# ABSTRACT BOOK

# iCBEI

## INTERNATIONAL CONFERENCE OF BIOMEDICAL ENGINEERING AND INNOVATION

## 24-26. 10. 2022, PÉCS

PÉCSI TUDOMÁNYEGYETEM
UNIVERSITY OF PÉCS

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# ABSTRACT BOOK

of the

**1st International Conference of Biomedical Engineering and Innovation**

University of Pécs
24-26. October 2022

**Edited by**
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# PROGRAMME OF
## 1ST INTERNATIONAL CONFERENCE OF BIOMEDICAL ENGINEERING AND INNOVATION

24.-26. October 2022
Szentágothai János Research Centre, 20. Ifjúság street, Pécs, Hungary

### MONDAY, 24. OCTOBER 2022

| | |
|---|---|
| 09:00–09:30 | Opening ceremony |
| 09:30–10:30 | **Metin Akay** - Novel NeuroTech for Addiction |
| 10:30–11:00 | Coffee Break |
| 11:00–12:00 | **Yasemin Akay** - Novel Therapeutics for Glioblastoma Multiforme (GBM) |
| 12:00–13:00 | **Gabor Forgacs** - Commercial Applications of Biofabrication |
| 13:00–14:00 | **Istvan Ulbert** - Neurobionics in aid of brain research |
| 14:00–15:00 | Lunch |
| 15:00–16:00 | **Workshop 1** - Bioprinting and biofabrication / Virtual and augmented reality / Functional electrical stimulation |
| 16:30–17:00 | Coffee Break |
| 17:00–18:00 | **Workshop 2** - Virtual and augmented reality / Functional electrical stimulation |
| 18:00–20:00 | Wine tasting |

### TUESDAY, 25. OCTOBER 2022

| | |
|---|---|
| 09:00–10:00 | **Ali Tinazli** - Digitizing Human HealthPrecise Individual Health Diagnostics through Digital Metabolic Analysis |
| 10:00–11:00 | **Akos Jobbagy** - Movement analysis aids patient care |
| 11:00–11:30 | Coffee Break |
| 11:30–12:30 | **Janos Voros** - A Bottom-up Approach to Neuroscience |
| 12:30–13:30 | **Natalie Mrachacz-Kersting** - Brain-Computer Interface design |
| 13:00– 18:00 | EIT Health iDAY Hackathon |
| 13:30–15:00 | Lunch |
| 15:00–16:30 | **Workshop 3** - Surgical guides for dental implant insertion / Simulation-based medical and healthcare education / Bioimpedance |
| 16:30–16:50 | Coffee Break |
| 16:50–18:00 | **Workshop 4** - Surgical guides for dental implant insertion / Simulation-based medical and healthcare education / Bioimpedance |
| 19:00–00:00 | Gala Dinner |

### WEDNESDAY, 26. OCTOBER 2022

| | |
|---|---|
| 9:00 - 10:00 | **Ewaryst Tkacz** - Applications of Artificial Intelligence in Medicine – 20 years of experience |
| 10:00 - 10:30 | IEEE Student Association Speech - **Andre Cakici** |
| 10:30 - 11:00 | Coffee Break |
| 11:00 - 12:20 | Presentations on Healthcare software development, healthcare AI, big data |
| 12:20 - 13:30 | Lunch |
| 13:30 - 15:00 | Presentations on Bioprinting, biotechnology; Simulation education, surgery planning and operational medicine; Medical materials technology |
| 15:00 - 15:30 | Hackathon Pitch |
| 15:30 - 16:30 | Rewards and closing remarks |
| 13:00 - 15:00 | Hackathon |

# KEYNOTE SPEAKERS

**METIN AKAY**
Founding chair of the Department of Biomedical Engineering, Cullen College of Engineering, University of Houston

**YASEMIN M. AKAY**
Instructional Associate Professor at the Department of Biomedical Engineering, Cullen College of Engineering, University of Houston

**GABOR FORGACS**
George Vineyard Chair in Biophysics at the University of Missouri-Columbia, Chanderna-Stirkey Chair in Theoretical Physics at Clarkson University, Chief Scientific Officer at Fork & Goode, Inc.

**AKOS JOBBAGY**
Professor emeritus at the Department of Measurement and Information Systems, Budapest University of Technology and Economics

**NATALIE MRACHACZ-KERSTING**
Professor at The University of Freiburg, Freiburg

**ALI TINAZLI**
Chief Executive Officer - lifespin GmbH · Regensburg, Germany

**EWARYST TKACZ**
Head of the Department of Biosensors and Processing of Biomedical Signals, Faculty of Biomedical Engineering, Silesian University of Technology

**ISTVAN ULBERT**
Chairman of the Neurobiology Scientific Committee of the Hungarian Academy of Sciences

**JANOS VOROS**
Professor in the Institute for Biomedical Engineering of the University and ETH Zurich and head of the Laboratory for Biosensors and Bioelectronics

# ORAL PRESENTATION SESSIONS

## HEALTHCARE SOFTWARE DEVELOPMENT, HEALTHCARE AI, BIG DATA
SECTION 1

**Main chair:**

CSABA **HETENYI**

**Chairs:**

Peter **Bogner**

Peter **Maroti**

Andre **Cakici**

Marton **Balogh**

Balint **Glazer**

## BIOPRINTING, BIOTECHNOLOGY; SIMULATION EDUCATION, SURGERY PLANNING AND OPERATIONAL MEDICINE; MEDICAL MATERIALS TECHNOLOGY - SECTION 2

**Main chair:**

CSABA **HETENYI**

**Chairs:**

Zoltan **Ujfalusi**

Judit **Pongracz**

Peter **Maroti**

Andre **Cakici**

Marton **Balogh**

Petra Ibolya **Polgar**

Luca Fanni **Kajos**

# KEYNOTE

PRESENTATIONS

# MOVEMENT ANALYSIS AIDS PATIENT CARE

**Ákos Jobbágy**

*Dept. Measurement and Information Systems, Budapest University of Technology and Economics Budapest, Hungary*

## INTRODUCTION

Electronic devices can motivate patients during rehabilitation. Involving people in their own healthcare is hard but greatly improves the efficiency. Medical devices for home application let people assess their actual parameters and also provide medical doctors with more detailed information about their patients' state. Quantitative analysis of movement is difficult and usually requires expensive equipment and trained operator. The presentation outlines four simple movement analyzing devices requiring modest expertise. These devices have been used to assist neurologists.

## METHODS

Four devices will be outlined. The patented hemisphere-like tool, Huple®, can improve the balance ability of children with birth injuries. PAM is a passive marker-based movement analyzer. The Smart Nine Hole Peg Tester, sNHPT, is a simple device for assessing hand dexterity. x-IMU is a 3D inertial measurement unit able to characterize different limb movements.

## RESULTS

Huple makes possible the objective and quantitative assessment of the balance ability and also increases the devotion of children to take part actively in the habilitation. PAM has been used for decades to assess the finger tapping movements of Parkinsonians. The quantitative assessment is able to reveal subtle movement disorders in screening test. Thus medication can start in the early phase. It may slow down the progress of the disease which can also be monitored using PAM. The sNHPT was used to monitor the improvement in the hand dexterity of 12 hospitalized stroke patients (45–80 years old) during their rehabilitation. The arm and hand tremor of stroke patients (60 – 75 years old) were analyzed with x-IMU.

## DISCUSSION

The four devices help neurologists to objectively assess the actual state of their patients. Huple and sNHPT have been also used by patients at home. The home application especially motivates the users and increases the effectiveness of rehabilitation.

# NOVEL THERAPEUTICS FOR GLIOBLASTOMA MULTIFORME (GBM)

**Yasemin Akay**

*Instructional Associate Professor at the Department of Biomedical Engineering, Cullen College of Engineering, University of Houston*

## INTRODUCTION

Glioblastoma multiforme is a malignant intracranial neoplasm that constitutes a therapeutic challenge because of the associated high morbidity and mortality given the lack of effective approved medication and aggressive nature of the tumor.

## METHODS

This presentation is relevant to topics of glioblastoma tumor biology, original basic research, clinical trials based on the collected evidence regarding the challenging factors encountered during the current treatment protocols, and novel therapies including immunotherapy and targeted therapy with the variety of combinations of drugs/chemicals.

## RESULTS

There are four main factors implicated in the low efficacy encountered with investigational treatments: **(1)** blood-brain barrier; **(2)** immunosuppressive microenvironment; **(3)** genetic heterogeneity; **(4)** external factors related to previous systemic treatment that can modulate tumor microenvironment.

In this presentation, two types of investigational therapies have been classified and discussed which were immunotherapy and targeted therapy.

Immunotherapy included: **(1)** immune checkpoint inhibitors; **(2)** adoptive cell transfer therapy; **(3)** therapeutic vaccines; **(4)** oncolytic virus therapy.

Targeted therapy included tyrosine kinase inhibitors and other receptor inhibitors.

## CONCLUSION

It should be emphasized that, addressing the molecular landscape and resistant immunosuppressive nature of glioblastoma are imperative in further development of effective treatments.

# COMMERCIAL APPLICATIONS OF BIOFABRICATION

**Gabor Forgacs**

*George Vineyard Chair in Biophysics at the University of Missouri-Columbia, Chanderna-Stirkey Chair in Theoretical Physics at Clarkson University, Chief Scientific Officer at Fork & Goode, Inc.*

Biofabrication is a highly multidisciplinary endeavor: it is the joint application of the life, physical and engineering sciences to make a useful product. In this talk I will overview two distinct-looking applications of this manufacturing paradigm: bioprinting and cell-cultured meat. The present audience is familiar with the first, but less so with the second, although the overlap between these fields is significant. Bioprinting (a version of 3D printing with live material) is the application of biofabrication in medicine, from basic research to pharmaceutics and therapeutics. Cell-cultured meat, is the application of biofabrication in the food industry to solve outstanding challenges related to sustainability. Both bioprinting and cell-cultured meat have seen spectacular progress in the last two decades, both in academia and commercially. The number of researchers devoted to the topic and commercial entities in the space have grown dramatically. Publications on the topic have been multiplying exponentially. However, as with most new technologies, due to the unavoidable hype, expectations have been set unrealistically high. This talk will also attempt to separate hype from reality, motivated by the desire to place these fields in the right perspective. This will be done by first briefly overviewing some of the fields' most remarkable accomplishments using illustrative and representative examples. Finally, an unbiased view on the future of bioprinting and cultured meat, will be presented, as much as this is possible by someone who has been involved in both fields essentially from their start.

# WORKSHOP

PRESENTATIONS

# BIOIMPEDANCE

**Instructors:** András Füredi, Attila Tóth, György Eigner, Nina Győrfi, Odry Ákos, Vízvári Zoltán

Bioimpedance spectroscopy is an extremely fast and cost-effective non-invasive material testing technique, which may therefore be one of the most promising medical technologies, a system of interrelated procedures of our present times and that of the near future. Our research group aims to spread this method as widely as possible, including the INTRODUCTION of special biological measurements in medical diagnostics.

With respect to the expected fast and efficient measurement procedures on a large number and in many cases seriously pathogenic human biological samples, the INTRODUCTION of robotics with highly automatized procedures can significantly increase the diagnostic role and significance of this technique, even in daily routine examinations.

In connection with all of this, our Research Group carried out original inventions and technical developments in a wide spectrum of bioimpedance measurements, from cell culture measurements for patients participating in our robotic developments towards the standardization of the measurement process and its high degree clinical practice in hospitals. When inventing the automated measurement protocols, we also paid attention at ensuring the reproducibility in our research activities.

During this workshop, we would like to present some of the results achieved during the short existence of the Research Group.

# BIOPRINTING AND BIOFABRICATION

**Instructors:** Judit Pongrácz, András Dinnyés, Anna Sebestyén, Zoltán Veréb

Bioprinting performed using a great variety of cells or supplementing additive manufacturing-based techniques. Biofabrication is an innovative and promising strategy that is increasingly gains recognition in the medical and pharmaceutical industry. The ability of producing tissues and organs has paved the way to create artificial multi-cellular tissues/organs for better understanding cellular interactions and physiology, for identification of drug targets, for testing drug toxicity or even create custom made skin grafts or bones. This new technology is evolving constantly and even reached industries we wouldn't have thought possible including agriculture as well as fashion.

# FUNCTIONAL ELECTRICAL STIMULATION

**Instructors:** Mravcsik M [1,2,3] . Zentai M [1], Laczko J [1,2]
*[1] Faculty of Sciences, University of Pecs, Hungary, [2] Wigner Research Centre for Physics, Budapest, Hungary, [3] National Institute for Medical Rehabailitation, Budapest, Hungary*

## INRODUCTION

We present functional electrical stimulation (FES) techniques and protocols for basic and clinical research. Especially FES assisted cycling movements of paraplegic persons are discussed. With the FES technology, paralyzed muscles can exert active muscle forces to perform a motor task. In particular cycling movements of spinal cord injured patients are generated and controlled by FES for physiological wellbeing of the patients. Muscle stimulation patterns are defined and using these patterns the muscles' activity are artificially controlled and coordinated. FES cycling (tricycling) is used not only for therapy but also there are cycling competitions for spinal cord injured persons, whose lower limbs are paralyzed.

## METHODS

Stimulation patters are based on measurements performed on able-bodied young participants. 3D movement analyzing systems are used to record joint coordinates, crank angle position by ultrasound based sensors, and muscle activities (electromyograms) by surface electrodes. Then the range of activities of the individual muscles are presented as function of crank angle. In the case of spinal cord injured patients each muscle is stimulated via surface electrodes in the proper range of crank angles, by sequences of electrical impulses. The amplitude, frequency and pulse width of these impulses can be adjusted. Blood pressure, heart rate, and cycling performance, as power output and energy output was monitored.

## RESULTS

We investigated the efficiency of FES cycling trainings of spinal cord injured paraplegic patients. The participants were able to cycle for 20-30 minutes using FES. Their blood pressure and heart rate increased after the beginning of the training and dropped to the resting level after the training. Their power output depended on the level of spinal cord injury and also on the number of stimulated muscles. It increased during the course of the training sessions.

## DISCUSSION

The FES assisted cycling training has beneficial effects on the physical performance, e.g. power output, cycling speed, and physiological parameters e.g. heart rate, blood pressure of spinal cord injured, paraplegic patients who would not be able to generate active muscle forces without FES. This method should be used in regular rehabilitation protocols. FES cycling is an important event at the Cybathlon competition as well, that is a competition of technology developers, engineers and participants with physical disabilities. This study may contribute to our participation on such events.

## ACKNOWLEDGMENT

Supported by the grant GINOP 2.3.3-15-2016-00032 of the University of Pecs, and by the Pázmány Péter Catholic University

# SIMULATION BASED MEDICAL AND HEALTHCARE EDUCATION - A HANDS-ON WORKSHOP

**Instructors:** Szilárd Rendeki, Bálint Nagy, Bence Szélig, Márton Németh, Martin Rozanovic, Mihály Csont, Péter Szűcs, Viktor Bacher

This workshop will explore functional electrical stimulation (FES) techniques and protocols for basic and clinical research. Furthermore this workshop will discuss the applications of these techniques in rehabilitation of spinal cord injured patients. Especially FES assisted cycling movements of paraplegic persons will be discussed. With the FES technology, paralyzed muscles can exert active muscle forces to perform cyclic limb movements. It will be presented, that how stimulation patterns are defined and how the muscles' activity can be artificially controlled and coordinated. The effect of the FES assisted cycling trainings on the physical performance, e.g. power output, cycling speed, and physiological parameters e.g. heart rate, blood pressure will be presented. FES cycling (tricycling) is used not only for therapy but also there are cycling competitions for spinal cord injured persons, whose lower limbs are paralyzed. FES cycling is an important event at the Cybathlon competition that will also be discussed at the workshop.

# SURGICAL GUIDES FOR DENTAL IMPLANT INSERTION

**Instructors:** DentUpgrade, Attila Csenki, Gyula Marada, Zsolt Rajnics, Vér Tamás

Dental restorations made with the help of various dental implants are becoming more and more popular and accessible in dentistry as well. However, the insertion of implants can have many difficulties, such as the lack of quantity and quality of the bone, or the various anatomic conditions. In these cases, the use of different surgical templatesor surgical guides can help, and by the using of these guides possible difficulties can be successfully overcome.

The aim of the workshop is to present a digital system that plans the exact spatial position of the dental implant to be inserted using the most modern 3D diagnostic methods (Cone Beam Computer Tomography). The surgical template prepared accordingly guarantees that the implant will be inserted exactly in the planned position. During the workshop, with the help of real CBCT recordings, the entire workflow is presented, from design to 3D printing of the surgical guide.

# VIRTUAL AND AUGMENTED REALITY (VR/AR) IN BIOMEDICAL AND STEM/STEM EDUCATION

**The workshop is co-organised with the contribution of our respected partners within the V.I.B.E. Erasmus+ project:** Politechnika Slaska, Dex Innovation Centre, University of Porto, Balázs Tukora, Péter Hillebrand, Péter Maróti

On this workshop, the participants get insight into the latest achievements of novel, innovative visualization technologies used for educational purposes. Experts from the field give a short summary about the most frequently used devices, displays and platforms, also, they highlight interesting use-cases from the field of bio-medicine and the disciplines of STEM/STEM. At the end of the lectures, it will be possible to explore the immersive and amazing world of AR and VR in a practical demo session!

# ORAL

PRESENTATIONS

# APPLICATION OF ARTIFICIAL INTELLIGENCE FOR IDENTIFICATION OF MEDICATION ERRORS: DEVELOPMENT AND TESTING OF AN OBJECT DETECTION MODEL FOR PILL RECOGNITION

**Amir Reza Ashraf [1], András Fittler [1]**

*[1] University of Pécs Faculty of Pharmacy, Department of Pharmaceutics, Pécs, Hungary*

## INTRODUCTION

Recognition of solid oral dosage forms (e.g. pills, capsules, tablets) based on their visual appearance is a regular challenge for patients and healthcare professionals worldwide. Advancement of artificial intelligence (AI) has enabled machines to perform complex tasks that would typically require human cognition, such as object detection and image classification, which can be a useful tool for solid oral medication recognition. Pharmacists working in community and hospital settings can potentially use these technologies in many areas including patient counselling, medication reconciliation, and to reduce medication errors caused by misidentification of medication by patients and healthcare professionals.

Our research aimed to develop and test an object detection model using machine learning for solid oral dosage form recognition.

## METHODS

A training dataset of 17920 images was built from 20 commonly dispensed medications in Hungary. These images were captured with a Sony IMX363 camera sensor with resolution of 12 megapixels under various conditions (lighting, distance, angle, dose container) and were imported into Microsoft Azure Custom Vision platform and used without augmentation to train our pill recognition AI model.

A validation dataset of 640 test images were captured under various conditions to test the model's performance. Accuracy, specificity, precision, recall, and F1 score evaluation metrics were calculated.

## RESULTS

Our model reached 98.9% precision, 93.6% recall and 98.5% mAP metrics in Azure after training, with probability and overlap thresholds set to 50% and 30% respectively under the reference condition. Confusion matrix of 640 real-world test images showed lower metrics overall, with 78.4% precision and 75.6% recall. Per-class (medication) precision and recall values both ranged between 43-100%. Furthermore, the model's overall performance showed promising metrics of 97.6% accuracy, 98.7% specificity and 75.7% F1 score.

## DISCUSSION

We have built a uniquely large dataset of training images from a limited list of regularly prescribed medications. To evaluate our model more rigorously, a completely separate image dataset was captured and used for testing to better correlate to real world predictive value of the model. High precision and high recall values indicate the model's lower tendency to make false positive and false negative predictions, respectively.

These results in line with previously published studies on medical image classification, indicate a promising potential for further development and performance improvement. Recognition of medications with similar appearance is a challenge for the human eye, with constant advances in the field of machine learning, soon it could serve as a valuable supportive tool for medication identification in community and hospital pharmacy settings.

# HUMAN EXPOSURE TO ULTRASONIC NOISE, BIOACOUSTIC

**Viktor Bagdán Dr., István Gyurcsek Dr., György Elmer Dr., Zoltán Kvasznicza Dr.**

*Faculty of Engineering and Information Technology,*
*University of Pecs, Hungary*

## INTRODUCTION

Currently, several countries have legislation limiting the permissible levels of ultrasonic noise. As technological progress has led to the INTRODUCTION of ultrasonic pollution in many areas, some countries have introduced restrictions. Ultrasound is used in underwater positioning, in industry (from 20 kHz), or in medical diagnostics (up to 10 MHz). It also includes various home devices, such as, but not limited to, burglar alarms, dog whistles, bird and rodent alarms, humidifiers, inhalers, or car-mounted animal alarms. As early as the 1940s-1950s, the harmful effects of ultrasound in industrial areas were reported, with symptoms including hearing damage, thermal effects, subjective symptoms and functional loss.

Our goal with this research is to highlight the importance of considerations the harmful biomedical effect of ultrasonic noise to the human health in comparison with international offers and regulations.

## METHODS

During our experiments, measurements are made on various medical instruments (dental drills, ultrasonic depurators) using a special measuring device designed for this purpose. The equipment is calibrated using a sound pressure level meter with factory calibration.

A ZOOM H1 digital sound recorder was used to record the noise, to which a special MEMS microphone (type: SPU0410LR5H-QB) was connected. This microphone is specifically designed for ultrasonic operation, allowing measurements up to 80kHz. Our complete measurement system can currently record signals up to 45kHz (the limitation is caused by the ZOOM H1). Before the measurements, a laboratory signal generator and an ultrasonic loudspeaker were used to verify that the measurement system was capable of recording ultrasonic signals. After calibration of the measurement system, measurements were started.

## RESULTS

During our measurements, we recorded high, and in the long-term dangerous levels of ultrasonic range noise during dental depurator measurements. The depurator is used to remove calculus.

Our evaluations and conclusions are based on the selected range of measured objects only they are to be extended in the following phases in research to prove our measuring results and the importance of the direction of international regulations in this field.

## DISCUSSION

Our research aims to find out whether ultrasound noise pollution in office environments, industrial environments and near medical instruments is of such a magnitude that it could have adverse health effects.

# A SOFTWARE-BASED SEGMENTATION OF MOIRÉ FRINGES OF SCOLIOTIC SPINES

**Csaba Bogdán**

*Medical School, University of Pécs, Hungary*

## INTRODUCTION

In 1970, as one of the first techniques applied in clinical diagnosis in topographic analysis, moiré topography (MT) was proposed for examining the shape of objects in three dimensions [19]. MT is based on optical phenomena by which moiré images (MIs) are created, comprising alternating bright and dark fringes. The pattern formed by moiré fringes (MFs) on the surface of an object is then applied for subsequent analysis. The primary advantages of MT are that it is non-invasive, fast, free of harmful radiation, portable and cost-effective. MT is used for detection of early stages of scoliosis and different deformities of the spine. However, further research is required to improve the analysis of the topograms. For reducing uncertainties in MF analysis, an accurate segmentation of MFs is needed for which the concept and prototype of a software-based Moiré Fringe Segmentation Tool (MFST) was developed.

## METHODS

The principle of operation of the software follows a manual/semi-automatic solution for MF detection. Software features and key functions are defined by filtering and morphologic image processing operations (FMIPO). The key elements of the concept of MFST consist of (1) field of FMIPO, (2) button bar for built-in algorithms for supporting manual fringe detection (3) panel for previewing image processing phases and (4) standard buttons. Base package of FMIPO covers adjustable parameters for brightness, contrast, thresholding, and to apply filters as 2-D Gaussian blur and skeletonization.

## RESULTS

MFST allows a dynamically changeable and user-friendly processing configuration on MIs created with XOR logic. The application-supported quasi-real-time segmenting method is simple, fast to process and, for the most part of the MIs follows the MFs accurately. The GUI of MFST consists of four main areas: (1) image canvases for original reference and processed image, (2) image processing toolbar, (3) toolbar for displaying skeletonized results and (4) built-in automatic segmenting algorithms. Although the solution used includes a rather narrow set of FMIPOs, it still allows for a visually traceable and relatively accurate delineation that may even be used for specific measurements.

## DISCUSSION

FMIPOs—although they make adaptive and flexible segmenting process possible—can lead to data loss, and thereby to inaccurate and sporadic contours. A possible way of improving the fringe segmenting application is to extend its functions with further operations such as (1) dilation for gradually enlarging the boundaries of regions of foreground pixels, (2) high-pass filters for image sharpening, (3) adaptive thresholding with local mean and global mean values.

## ACKNOWLEDGMENT

I would like to express my gratitude to Salus Orthopedtechnika Kft. (István Joó, Katalin Prommer, Ferenc Marlok) for providing sample images to this research.

# PICUR: IMPROVED UV INACTIVATION DEVICE FOR RESEARCH AND DIAGNOSTIC USE

**Roland Hetenyi, Daniel Hanna, Edina Szabó-Meleg**

*Pharmacological and Pharmaceutical Sciences, Medical School, University of Pecs, Hungary*

## INTRODUCTION

Highly infectious pathogens require high biosafety precautions that seriously restrict research and pose a threat to diagnostic personnel. Working with highly infectious pathogens at lower biosafety levels can expedite research yet requires the pathogen to be completely inactivated. UV-C irradiation is highly effective in inactivating pathogens. Current technologies handle continuously flowing complex materials or use an additive to UV-inactivate blood products. No device is ready for direct homogenous irradiation of microcentrifuge tubes or blood collection tubes.
RoLink Biotechnology's improved UV-inactivation device is a proposed medical device intended to reduce the pathogen load or inactivate pathogens in cellular or cell-free media and serum or plasma. The device is designed to add an extra layer of safety to research and diagnostic procedure, eliminating infectious pathogens.

## METHODS

We designed a device specifically for research and diagnostic use. The prototype was tested to inactivate SARS-CoV-2 in a BSL-4 laboratory. Complete inactivation was validated by cytopathic effect, PCR, plaque assay, and dsRNA. Proteomic analysis was performed using SARS-CoV-2 RBD and S1 ELISA kits.

## RESULTS

SARS-CoV-2 is completely inactivated in under 30 seconds. There were no plaques or cytopathic effects compared to the active control, RT-PCR and PCR showed no RNA replication, and immunofluorescence of dsRNA showed no sign of replication. No in vivo replication occurred in a Syrian Hamster model. The proteomic analysis demonstrated that the UV-inactivated virus is capable of the same endocytic process. ELISA confirmed no significant difference ($p<0,05$) between the active and inactivated virus in RBD and S1 proteins.

## DISCUSSION

We demonstrated that RoLink Biotechnology's improved UV-inactivation device is applicable in BSL-3 and BSL-4 laboratories; experiments are feasible in biosafety cabinets and can be integral parts of routine virological laboratory procedures. Downstream research of the completely inactivated BSL-3 pathogen SARS-CoV-2 can be routinely executed in a BSL-2 environment. UV-inactivated SARS-CoV-2 is suitable for all non-propagative laboratory work, including immunological, proteomic, and molecular biological applications. Regarding cost savings, immunological research carried out in a BSL-2 environment required 60% fewer personnel, carried 0% infectious hazards, and cost 80% less compared to the available BSL-4 facility on site.

## ACKNOWLEDGMENT

The research was performed in collaboration with the National Virology Laboratory, University of Pécs. The project 2020-2.1.1-ED-2020-00100 was sponsored by the National Research, Development, and Innovation Office of Hungary.

# LOCOMOTION SYNTHESIS WITH DEEP REINFORCEMENT LEARNING AS A SIMULATED TESTBED FOR WEARABLE ROBOTIC DEVICES

**Balint K. Hodossy, Dario Farina**

*Department of Bioengineering, Imperial College London, United Kingdom*

## INTRODUCTION

Inefficient control schemes of robotic lower limb Prosthetics and Orthotics (P&O) limit the number of cases where they are a worthwhile intervention. Access to hardware, participants, and versatile test environments make testing novel control concepts difficult. The use of virtual simulation testbeds in the iterative design cycle can speed up this process. However, a key challenge in this application is the closed-loop simulation of the user's movement, necessary to provide the kinematic and kinetic context for the tested device.

Deep reinforcement learning agents can learn robust gait policies in diverse environments, with human-like movement. This study investigates the suitability of a proximal policy optimization-based motion tracking method in simulated P&O settings.

## METHODS

A kinematic gait synthesizer is built using motion-matching, generating level-ground walking, turning and pivoting reference motions for a dynamic, torque-actuator based humanoid model simulated in the MuJoCo physics engine. Transtibial prostheses, with different impedance control strategies were investigated, including finite-state-machine and reinforcement learning based methods.

## RESULTS

Aspects of the gait cycle, such as ground reaction force curves and stance phase ankle dynamics emerged naturally despite not specifying them in the reward function. While healthy participant reference data were used, gait asymmetry comparable to literature values were measured when a virtual prosthesis was used.

## DISCUSSION

Using simulated gait and devices, the complex design space of P&O can be explored in a low-cost and accessible way, promoting the transfer of the next generation of device controllers from the lab to real life scenarios.

## ACKNOWLEDGMENT

This work was partially supported by the UKRI CDT in Prosthetics and Orthotics (Grant No. EP/S02249X/1) and the Natural BionicS initiative (Grant agreement ID: 810346).

# PREDICTIVE VALUE OF DIFFUSION PARAMETERS USING ARTIFICIAL INTELLIGENCE IN LOW-AND INTERMEDIATE-RISK PROSTATE CANCER PATIENTS TREATED WITH STEREOTACTIC ABLATIVE RADIOTHERAPY

**András Kedves[1,2,3], Metin Akay[4], Yasemine Akay[4], Ting Chen[4], Katalin Kisiván[1], Csaba Glavák[1], Ádám Schiffer[2], Aba Lőrincz[2,4], András Szőke[2,8], Árpád Kovács[3,6,7], Ferenc Lakosi[1,3,6]**

**1** "Moritz Kaposi" Teaching Hospital, Dr. József Baka Diagnostic, Radiation Oncology, Research and Teaching Center, Kaposvár, Hungary
**2** Institute of Information and Electrical Technology, Faculty of Engineering and Information Technology, University of Pécs, Pécs, Hungary
**3** Doctoral School of Health Sciences, University of Pécs, Pécs, Hungary | **4** Department of Biomedical Engineering, University of Houston, Houston, TX, USA | **5** Institute for Translational Medicine, Medical School, University of Pécs, Pécs, Hungary | **6** Department of Medical Imaging, Faculty of Health Sciences, University of Pécs, Pécs, Hungary | **7** Department of Oncoradiology, Faculty of Medicine, University of Debrecen, Debrecen, Hungary | **8** 3D Printing and Visualization Center, University of Pecs

## INTRODUCTION

To investigate the predictive value of the pre-treatment diffusion parameters of diffusion weighted MRI using artificial intelligence (AI) for PSA response in patients with low- and intermediate-risk prostate cancer (PC) treated with stereotactic ablative radiotherapy (SABR).

## METHODS

Retrospective evaluation was performed using pretreatment multiparametric MR image datasets of 40 PC patients between 2017 and 2021. MR based mean- and minimum apparent diffusion coefficients (ADCmean, ADCmin) were calculated for the intraprostatic dominant lesion where it was visible. Therapeutic response was assessed using prostate-specific antigen (PSA) levels. Two patient subgroups were created, divided by the median of the last PSA measurements. Two different prediction models based decision tree (DT), and random forest (RF) classifiers were established. Predictive performance was assessed by the receiver operating characteristic (ROC) analysis. For statistical analysis, Spearman's correlation and Wilcoxon's signed-rank test were used, with a significance level of $p \leq 0.05$.

## RESULTS

No biochemical relapse was detected after a median follow-up of twenty-three months (range: 3–50), with a median PSA of 0.01 ng / ml (range: 0.006–2.8) at the time of the last examination. PSA nadir has not yet been achieved in 45% of patients. There were no significant correlations between time-to-nadir and ADCmean, ADCmin ($r = -0.3165$, $p = 0.0600$ and $r = -0.3149$, $p = 0.0613$). Although, moderate negative correlations were found between ADCmean, ADCmin and PSA nadir values ($r = -0.5678$, $p < 00001$ and $r = -0.5633$, $p < 0.0001$). Furthermore, significant differences were observed between the pretreatment ADCmean, ADCmin parameters, and the subgroup averages of patients with low and high PSA nadir measurements ($p = 0.0022$ and $p = 0.0021$). The ML data of PC patients were classified into a training set (20%) and to a validation set (80%). In prediction, the RF model outperformed the DT model, yielding area under the curves (AUC), with 0.766 and 0.700, respectively.

## DISCUSSION

Our findings suggest that pretreatment MR diffusion data may predict therapeutic response using novel approach of artificial intelligence. A higher number of cases and longer follow-ups are warranted.

## ACKNOWLEDGMENT

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# TELEMEDICINE: ADVANCING CASE MANAGEMENT FOR PATIENTS WITH DISABILITIES IN INDONESIA DURING THE OUTBREAK OF COVID-19

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## INTRODUCTION

Return to Work (RTW) as case management for handicapped social security beneficiaries raises concerns. However, research on the potential of turning telemedicine to be applied to the RTW program is underwhelming. This study aims to investigate the dynamic of telemedicine in implementation of the RTW Program as case management for disabled patients during the COVID-19 pandemic.

## METHOD

A qualitative study used claims data for work-related accidents from BPJS Ketenagakerjaan, Indonesia., followed by a semi-structured interview with 11 case managers who helped patients with disabilities during the RTW program with telemedicine. Claims data were evaluated descriptively and visualized using Python with ArcGIS interface. The findings from the semi-structured interview were assessed using the QDA Miner Lite program.

## RESULTS

The findings of this research include five primary themes, which are as follows: the adjustment disparity timeframe from the classical methods; boundaries to instituting telemedicine in healthcare providers; regulatory oversight litigation within the implementation of telemedicine; the potential advantage of leveraging telemedicine; and the complexities of telemedicine throughout the context.

## DISCUSSION

Despite significant concerns about telemedicine, the advantages should outweigh some of the experienced forms in managing cases involving disabled patients in Indonesia. Some issues of adjusting telemedicine for disability management must be addressed. Further research is necessitated to evaluate the effectiveness of telemedicine in case management for disabled patients in a RTW program.

## ACKNOWLEDGMENT

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# ONLINE ASSESSMENT OF MEDICAL MATERIALS IN THE LIGHT OF RESILIENCE

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## INTRODUCTION

The presentation aims at eliciting insight into the results of an ongoing research regarding evolving trends and attitudes towards online assessment of medical materials. The focus pinpoints online as one of the most trending forms available during and since the global pandemic.
The study was first initiated in 2019 in which its main target was to reveal the intriguing question of students' and assessors' attitudes towards online assessment of medical materials at the University of Pécs Medical School. The research aims at questioning and reviewing candidates' and assessors' attitudes and best practices towards online assessment since 2019.

## METHODS

Material and methods include surveys, needs and wants analysis and thorough investigations regarding candidates' and assessors' attitudes, fears and best practices towards online tests in the field of Medicine. The examined test tasks include various online tests drafted in both English and Hungarian by student volunteers at the Medical School of the University of Pécs, Hungary. Over 400 respondents from more than 28 countries participated in the survey, which gives us an international and intercultural insight into how students with different cultural and educational background deal with the evolving online world.

## RESULTS

The results show the pandemic's impact which brought the slumbering online world of assessing roaring alive, fully operational and now bears phenomenal relevance in today's global education. Undeniably, the results can be used as a perspective in a vast array of contents. Moreover, we intend to achieve results which can be an aid for actively assessing teachers and also for students desiring to improve their skills regarding medical materials aiming at an improving level to conduct a reliable and valid online assessment. The present findings confirm the need and value of online assessment; however, the concern of validity and technical issues provide a good starting point for discussion and further research for us to be able to move on to the next level.
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## DISCUSSION

The survey hypothesized the generation of the 21st century expect everything readily available online, however, questions whether they are ready for this challenge are lurking in the background. One of the characteristic goals in support of this study is to outline a comprehensive vision of the assessment of medical materials from varying perspectives, including context, time, place, tasks, test developing, technology and the question of validity of online assessment.

## ACKNOWLEDGMENT

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# EFFECT OF OZONE DISINFECTION ON MECHANICAL PROPERTIES OF 3D PRINTED MATERIALS

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## INTRODUCTION

The advancement of 3D printing offers a great tool for fast prototyping and small-scale manufacturing of laboratory equipment. Ozone treatment might be a candidate disinfecting instruments or tools used with cell cultures as ozone gas can enter the smallest gap.
While there are tables of ozone resistance of materials, classifying from A to E, but there are no data available how ozone treatment affects the tensile and flexural strength of 3D printed materials.

## METHODS

Test specimens described by ISO 178 and ISO 527-2 were printed in two orientations from ABS, ASA, PETG and PLA and treated with ozone once (20 minutes, 400 ppm), ten times or none (control). Tensile test and three-point flexural test were performed with a Mecmesin MultiTest-dV compression and tension test stand. The measured parameters were compared between the groups of same material and orientation.

## RESULTS

Visual inspection of the ten times treated test specimens did not reveal any degradation. The vertically printed PLA specimens showed a statistically significant, but small decrease in ultimate strength and increased Young's modulus in the ozone treated groups. There were no additional significant differences in the tensile or flexural strength between the tested groups (control vs one ozone treatment vs ten ozone treatments).

## DISCUSSION

Our results show that not even repeated ozone treatment affected negatively the tensile and flexural strength of most of the tested materials. A simple chamber with an added ozone generator can provide cheap and quick disinfection method for 3D printed components. The expansion of this study is planned with thermoplastic polyurethane (TPU 95A) and nylon (PA-6).

## ACKNOWLEDGMENT

We would like to thank Dávid Csonka for his helpful comments.

# THE EFFECT OF POSITIVE AND NEGATIVE LIFE EVENTS ON THE BRAIN USING NON CONTRAST BRAIN PERFUSION IMAGING

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## INTRODUCTION

It is proved, that positive and negative life events have major impact on brain structure, and function, especially in the age of 10-15 – when the plasticity of the brain is high. Positive events help the formation and the affirmation of the synaptic connections, whereas negative events block the formation of new synaptic connections and lowers the remodeling rate of the neuronal network. These may lead to quantify differences in the rate of brain perfusion, which goes with the change of the CBF (cerebral blood flow).

## METHODS

Magnetic resonance imaging was acquired using a 3T Siemens Magnetom Trio Tim scanner. Arterial spin labelling (ASL) sequence was used to quantify CBF. The subjects will be assigned into three groups: One will consist of subjects that studied music - as a positive life event - in the high plasticity period of their development. Another group will consist of subjects who grow up in an orphanage and the third group will consist of control subjects (24) that will be matched with age and sex.
During post-processing we will do segmentation, registration and the quantitative analyzation of the CBF with Matlab, followed by the statistical analyzes using SPSS.

## RESULTS

As the research is in the initiatory phase, we do not have exact results, but we foresee differences in the CBF between the two study groups compared to control subjects. Additionally, we would like to further improve the post-processing pipeline.

## DISCUSSION

We hope that the results will contribute to the wider understanding of neuronal processes in psychiatric disorders, and to the development of effective curing methods for this widespread disease.

# HUMAN IPSC-BASED 3D NEUROSPHERES AND MICROGLIA FOR DISEASE MODELLING AND TOXICOLOGY SCREENING

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## INTRODUCTION

The human induced pluripotent stem cell (hiPSC)-based 3D in vitro models' open new possibilities for toxicology and disease modelling. In this study, we developed a 3D hiPSC-derived neurosphere model to mimic brain architecture for toxicological screening. Differentiating neuronal cultures were exposed to various ultrafine particles to investigate their effect on cellular viability. This model is part of our ongoing efforts to be incorporated into microfluidic multi-organ-on-a-chip (MOOC) devices. Furthermore, a 3D differentiation protocol was established to generate iPSC-derived microglia-like cells.

## METHODS

Control and AD iPSC-derived neural progenitor cells were differentiated into neurospheres for 21 and 49 days, respectively then exposed to ultrafine particles and ATP-based viability assays were performed. iPSC-derived microglial cells were generated through a 3D differentiation protocol (Haenseler et al. 2017). The harvested cells were further cultivated in neurosphere co-culture for 4 weeks and evaluated using RT-qPCR, and ICC.

## RESULTS

Our experiments indicate that low concentrations of ultrafine particles did not affect cellular viability. The 3D neuronal-astrocyte-microglia co-culture model is suitable for further disease modelling and drug screening.

## DISCUSSION

Human iPSC-derived 3D neurospheres can be effective models for neurotoxicology, supporting or substituting animal models, especially when combined with microglia-like cells. Our in vitro co-culture system offers an enhanced recapitulation of AD pathology in vitro compared to monoculture-based systems and ready to be used in MOOCs.

## ACKNOWLEDGMENT

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# HUMAN INDUCED PLURIPOTENT STEM CELL-DERIVED CARDIOMYOCYTE BIOENGINEERING TOWARDS AN ADULT HEART MODEL

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## INTRODUCTION

Human induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CMs) are important tools for developing cardioprotective drugs and in vitro cardiotoxicology. Existing protocols generate foetal-like CMs, characterized by glycolytic metabolism, spontaneous beating, circular cellular shape, lack of sarcomere alignment, expression of foetal genes and isoforms of calcium handling and contractile proteins. The need of the industry is to use adult-like CMs.

## METHODS

We developed a differentiation protocol from hiPSCs to induce CM development. Most of the characteristics are foetal-like, including gene expression profiles, isoforms, metabolism, cell size and morphology. In order to induce cardiac maturation, with our partners in the EU H2020 EMAPS-Cardio project we are developing a complex system where the hiPSC-CMs are placed on a 3D cellular-scaffold system and stimulated in various ways (electrical, mechanical, biochemical, topological) in a controlled bioreactor environment.

## RESULTS

We have successfully developed spontaneously beating hiPSC-CMs, with characteristic features of the foetal heart cells, as shown with immunocytochemistry, PCR and FACS experiments. Electrophysiological characterization was performed using patch clamp, sharp electrode measurements and multielectrode array recordings.

## DISCUSSION

The obtained cellular system will need to be exposed to a microenvironment in order to stimulate further maturation and to obtain a more accurate human-relevant in vitro model with high translational value of drug development and cardiotoxicity safety and to replace animal models.

## ACKNOWLEDGMENT

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# ROAD TYPE RECOGNITION WITH SMARTGLASSES AND MACHINE

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## INTRODUCTION

Driving a car is an activity that has become necessary for exploration of the present world. Research on road safety are among the important ones. In this article, we propose an algorithm based on machine learning algorithm for the recognition of four common road types based on physiological signals from JINS MEME ES_R smart glasses (electrooculography, acceleration and angular velocity). Data from 30 drivers were obtained in real driving conditions. Handcrafted statistical features were extracted from the physiological signals for training validation and testing of a random forest classifier. We have achieved overall accuracy, precision, reminder, and an F1 score of over 87% on the test dataset.

## METHODS

Data were acquired under real road conditions from 30 healthy subjects, including 20 experienced drivers and 10 students attending a driving school. All data were labeled during the drive and then divided the into four groups regarding the type of the road (1: highway; 2: city road; 3: undeveloped area; 4: housing estate). The data were then denoised using median filter and normalized using min-max normalization. The features (minimum, maximum, skewness, kurtosis, μ, and □ ) were calculated on 100 sampled windows with a stride of 50 samples for each signal. The feature extraction process resulted in 36,669 feature vectors of 48 dimensions (6 features for each of the 8 sensor channels) that were used to train, validate and test the classifiers. Finally, feature selection was also performed using ANOVA on each feature separately to determine which ones maximized the distance between the four classes we used in our problem. For the classification we used random under sampling boosted trees with Bayesian hyperparameter optimization process.

## RESULTS

We calculated some standard evaluation metrics computed from the confusion matrix of the classifier. The classifier achieved overall accuracy 87,65%, precision 86,30%, recall 88,12% and F1-score 87,08%. Additionally the model scored above 97% AUC for each class. This relatively high accuracy indicates that physiological data acquired from JINS MEME smart glasses (EOG, acceleration and angular velocity) are sufficient to determine the type of road being traveled.

## CONCLUSSION

WStatistical features were manually extracted from the data and used to train a classifier for the recognition of four different road types (city road, highway, housing estate and undeveloped area). A comparative study between various state-of-the-art classifiers was carried out and led to a best overall accuracy of 87.64\% using boosted trees. Additionally, a feature importance calculation based on ANOVA showed that the most important features were coming from head movements.

## ACKNOWLEDGMENT

Doniec R, Piaseczna N, Li F, Duraj Konrad, Hozhabr Pour H, Grzegorzek M, Mocny-Pachońska K, Tkacz E, „Classification of Roads and Types of Public Roads Using EOG Smart Glasses and an Algorithm Based on Machine Learning while Driving a Car” ,Electronics 2022, 11(18), 2960;

# SUPPORTING THE PROCESS OF REHABILITATION OF COGNITIVE FUNCTIONS USING THE XBOX GAME

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## INTRODUCTION

Human cognitive functions can be defined as a set of skills that allow us to collect data, analyze it and respond appropriately based on previous analysis. They play an important role in human life, allowing us to function normally. Impaired cognitive functions lead to difficulties in the life of a person affected by this dysfunction. Due to the low degree of neurogenesis and the progressive degree of neurodegeneration, the elderly are often affected by this condition.
The aim of the study was to develop a game using synergy between intelligent image processing, a state-of-the-art 3D vision device and gamification methods to improve the effectiveness of cognitive function rehabilitation for seniors.

## METHODS

An important element considered during the development of the application was to adapt it appropriately to the needs of the elderly. For this reason, we decided to create a game world reflecting a friendly environment with a clear interface suitable for the elderly. For this purpose, we used a large fonts, as well as colors that create a high contrast between each other. The gameplay menu was created in such a way that using it is intuitive.
After consultation with experts and analysis of literature, the first attempts were made to develop rehabilitation scenarios and implement the game. We decided to base on popular game, consisting catching the right objects with hands and avoiding unbeatable objects. By using depth sensors and developing software it was possible to create a game that combines elements of motor exercises and data analysis. The player analyzes the received data, then makes a decision to catch or not the objects through gameplay that provides necessity of movement. Gamification elements were also added to the game to further motivate the player: bonus system, level system and point system. During the gameplay we recorded a series of information to indicate patient's progress in rehabilitation: position of hands during the game, time of game, total number of objects, correct strokes, time between appearance of the objects and its nailing, points.
The project resulted in an implementation of a properly working game using depth sensors, allowing the rehabilitation of cognitive functions with special attention to the needs of the elderly. It allows to add variety to the rehabilitation process, and by recording the information about gameplay it is possible to later analyze its impact on the process of rehabilitation.

## DISCUSSION

The game has not been clinically tested, which, however is anticipated in the future. The results discussed here are based on theoretical predictions and tests on team members. We believe that the use of modern technology support of traditional way of rehabilitation will allow for greater efficiency and a shorter time in the process.

# 3D BIOPRINTED IN VITRO HUMAN TUMOUR MODELS IN ANTI-METABOLIC DRUG TESTS

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## INTRODUCTION

Cancer as a dynamic ecosystem reorganises the cellular microenvironment during tumour tissue evolution. Failures in cancer therapies highlighted that even the same tumours have site-dependent differences in nutrient/oxygen supply and related metabolic rewiring. These contribute to tissue heterogeneity, metabolic plasticity and adaptation. 2D, 3D cultures and xenograft models are used in basic research and pharmaceutical developments influencing pre-clinical drug selections' effectivity.

## METHODS

Establishing more representative in vitro 3D environment in cancer metabolism and drug research new 3D bioprinted, long-term in vitro cultures have been developed using different tumour cell lines (breast, central nerve system, lung and kidney cancer cells). 2D, 3D spheroid, hanging drop, 3D bioprinted and xenograft models and the heterogeneity of the growing breast cancer cells in correlation with their metabolic enzyme expression pattern and metabolic inhibitor and drug sensitivity have been compared using cisplatin and metabolic inhibitor treatments, tumour growth analyses, morphology, immunohistochemistry and WES Simple analyses.

## RESULTS

The established new 3D bioprinted tissue-mimetic structures provide more similarities in morphology (confocal microscopy – lumen formation), protein expression profiles (especially the analysed metabolic proteins), drug responses (chemotherapy and metabolic inhibitor treatments) and tissue heterogeneity than other in vitro breast cancer models.

## DISCUSSION

Based on our studies, the established 3D bioprinted tissue-mimetic structures provide further steps in representing in vivo 3D situations in in vitro drug toxicity/sensitivity tests and tumour metabolism research, suggest tissue mimetic structures replacing animal experiments. Additionally, these human cancer cell-based models can increase the success rate of drug pre-screening and future phase trials.

## ACKNOWLEDGMENT

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# USING GLUCOSE-OXIDASE BASED AMPEROMETRIC BIOSENSOR IN PRECLINICAL RESEARCH

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## INTRODUCTION

Measuring metabolic processes in the brain with adequate temporal resolution is crucial to understand its function. Based upon the presence of a glucose transporter within the prefrontal cortex, as well as previous studies showing the preventive effect of glucose drinking on the development of posttraumatic stress disorder (PTSD) we hypothesized that brain glucose metabolism, especially in the prefrontal cortical area, plays a crucial role in the development of the symptoms.

## METHODS

To test this hypothesis first we developed a biosensor, which can measure the glucose level within the brain with high temporal resolution. We tested it in an anaesthesized rat. In parallel, the peripheral glucose levels were followed by a commercially available tissue glucose sensor.

## RESULTS

We successfully optimized the size, lifetime and sensitivity of our electrode, which made it suitable for brain measurement in contrast to the commertial sensor (which is too flexible, not focused enough and not sensitive below 2mmol/l). After in vitro calibration our sensors were tested in vivo to prove their usability in animal models. The measurements were performed by periodically interrupted amperometry utilizing glucose oxydase.

## DISCUSSION

Our further research using this biosensor can contribute to the understading of the metabolic aspects of PTSD, therefore, to improve the efficancy of its therapy. The knowledge gained during development of the biosensor will open a new window for applying this electrochemical method to other projects and animal models. Indeed, this method is a versatile tool for preclinical research, because of the wide variety of possible target molecules (depending on the enzyme used).

The research is supported by PTE ÁOK-KA-2020-10,

# DEVELOPMENT OF INTRAOPERATIVE AND POSTOPERATIVE 3D RECONSTRUCTION METHODS IN IDIOPATHIC SCOLIOSIS CORRECTION SURGERY

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## INTRODUCTION

The surgical treatment of adolescent idiopathic scoliosis by transpedicular screw fixation spondylodesis involves the implantation of fixation rods on both sides of the spine. The aim is to develop a 3D reconstruction method which can evaluate the spatial deformation of the implanted rods and compare the intraoperative and the postoperative states.

## METHODS

To record the spatial position of the fixation rods during the surgery, an industrial 3D scanner Artec Eva was used. This allowed to obtain a point cloud with 0,1 mm spatial accuracy. The raw 3D models of the rods were completed in a professional CAD software as well as the postoperative 3D models using stereoradiographic images of the EOS® 2D/3D X-ray Imaging System.

## RESULTS

10 patients were involved in the study, and the largest resultant displacement measured was 26.1 mm compared to the intraoperative condition.

## DISCUSSION

A certain amount of correction loss can be expected after the intervention, which is assumed to reach a constant value over time. Rods bent by manual force and the corrected curvature of the patient's spine are also subject to significant forces that can lead to deformity. None of the rods maintain their pre-set shape, which is compounded by the fact that with the torsional forces within the human body at rest, patients are put on their feet after a week, which puts further load on the fixation rods, this can further increase the loss of correction. Combining the reconstructed intra and postoperative models it is possible to quantify this correction loss.

# POSTER

PRESENTATIONS

# CUSTOM LOWER LIMB PROSTHETIC DEVELOPMENT AND ANALYSIS

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## INTRODUCTION

Through recent studies, many technological tools have been developed, for example, computer-aided design and finite element analysis. Here we focus on the lower limb prosthetic and how to use the development of the methods in order to obtain the maximum comfort. Most of the components (e.g., foot and knee) can be selected from a standard catalog, while the socket must be designed and configured based on the patient's anatomy using these developments of CAD FEA.

## METHODS

The main objective of this project is to develop a digital model of the amputee to be ready for design and testing of the prosthesis in a fully virtual environment. To achieve this goal of replacing the traditional method with a virtual one, we have three stages: Data Collection, in which the patient will undergo 3D Scanning in order to obtain the perfect shape of the residual limb. The product design, which is the data collected, will go through a few stages of design according to the shape and size of the residual limb. Finite Element Analysis, in which the final design will be subjected to a strength analysis according to its variables to find the limits of stress, strain, strain and total deformation.

## RESULTS

The study clarifies the importance of CAD-FEA in developing the lower limb prostheses. We can see from the results of FEA that the designed socket was close to the expected one after some modifications based on the results of the FEA.

## DISCUSSION

Socket manufacturing using modern methods is the main key to obtaining an accurate socket relative to the shape and size of the residual limb, as well as facilitating and reducing the time for socket formation.

# RETINOIC ACID TREATMENT INDUCES KERATINOCYTE MARKER EXPRESSION IN 3D BIOPRINTED HACAT CELL LINE

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## INTRODUCTION

Skin tissue models are widely used models in toxicology testing. The suitability of these models is partly determined by specific gene expression markers. Our aim was to investigate the expression of two keratinocyte specific gene markers in 3D bioprinted (Cellink Bioink) Hacat cell line treated with Retinoic acid.

## METHODS

To investigate the effect of Retinoic acid treatment, 3D bioprinted (BioX Bioprinter, Bioink, Cellink) Hacat human keratinocytes were cultured for 48 hours, then treated with retinoic acid (2 nM) for 24 hours. Using the alginate bioink, 4mm thick structures were printed, and incubated in DMEM medium, supplemented with 10% FBS, 37 oC, 5% CO2. Gene expression of keratinocyte markers was evaluated by SYBR Green qRT-PCR.

## RESULTS

The detected gene expression changes can confirm the induction of keratinocyte differentiation. Both investigated differentiation markers (Filaggrin, Keratin1) showed increased levels of gene expression in the 3D bioprinted kerationcytes.

## DISCUSSION

This structure seems to be suitable for further studies, as the retionoic acid treated cell line started to differentiate. The study shows significant differences in retinoic acid treated Hacat cell line in contrast to the control cells. Such models will make our further tissue differentiation studies and drug testing experiments possible.

# APPLICATION OF MULTIPLE AAV SEROTYPES AND EXPERIMENTAL SETUPS FOR INHIBITION OF FOOD INTAKE BY SILENCING LHA USING DREADD TECHNOLOGY

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## INTRODUCTION

Designer Receptors Exclusively Activated by Designer Drugs (DREADD) is a novel chemogenetic technology providing temporally and spatially selective activation or inhibition of target cells.

## METHODS

We injected adeno-associated virus vectors (AAV5 or AAV9) expressing the gene of modified human M4D(Gi) cholinergic receptor, or PBS into the LHA of rats. We examined dose-response curves of clozapine-N-oxide (CNO) and deschloroclozapine (DCZ) after subcutaneous (s.c.) or per os (p.o.) administration in a food-intake paradigm. Rats were fasted for 16 h before the experiments, then, after re-feeding, we measured food consumption in the first 30 min and in every hour over an 8-hour long period. To conclude about the time-course of the actuator's effectiveness, intermediate dose of DCZ was injected s.c. at 16, 3, 1 or 0.5 hours prior to re-feeding time.

## RESULTS

All three doses of CNO administered s.c. and DCZ either s.c. or p.o. reduced food-intake measured at 30 min and 8 h time points both in the AAV5 and AAV9 groups but were ineffective in the PBS group. AAV5 and AAV9 injected animals consumed more food in the first 30 min when DCZ was given at 16 h prior compared to 0.5 or 3 h pre-treatment time point. All animals maintained their body weight between experiments, so the inhibitory effect was transient and solely caused by the actuators.

## DISCUSSION

We have proven the feasibility of DREADDs for reversible inhibition of food-intake. We aim to apply multiple titres of AAV2 to investigate possible neurotoxic side-effects before applying the technology for further experiments resembling cognitive decline.

## ACKNOWLEDGMENT

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# MODELLING LYMPHANGIOLEIOMYOMATOSIS IN 3D SPHEROID CULTURE

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## INTRODUCTION

Lymphangioleiomyomatosis (LAM) is a highly vascularized rare progressive multisystem disease that primarily affects women of reproductive age. LAM is characterized by aberrant, proliferating smooth muscle-like cells (LAM cells) and results in cystic deterioration of the lungs, chylous effusions and lymphangioleiomyomas. Dysregulation of the mechanistic Target of Rapamycin (mTOR) signaling pathway is the main cause of LAM cell proliferation consequently the mTORC1 inhibitors such as rapamycin are the only FDA approved treatment for LAM.

As not all patients can tolerate the long-term use of rapamycin, and the cessation of the therapy causes further and faster loss in lung function, further, more detailed study of the disease is necessary. The better understanding of the disease mechanisms requires a valid human model that can mimic the pathology and drug response of the rare LAM disease.

## METHODS

Patient derived LAM cells and normal human lung fibroblast (NHLF) cells were cultured in monolayer using cell type specific media. The cultures were trypsinized and the two cell types were seeded into a 96-well U-bottom plate (10,000 cells per well), then centrifuged for 5', 600rpm, at room temperature.

The aggregated spheroids were cultured for 3 days, then used as control, or treated with 20 nM concentration of rapamycin. Cell viability was determined by CelltiterGlo (Promega), while tissue sections were stained with fluorescently labelled alpha-smooth muscle actin (□-SMA) antibodies, where nuclei were visualized with DAPI.

## RESULTS

Tissue sections of the spheroids revealed that only LAM cell line containing spheroids revealed characteristic cysts in the structure while those were not present in the controls. Additionally, LAM spheroid obtained from fluorescent microscopy showed that the structure of rapamycin-treated LAM spheroids was disrupted, and the outer phase was decaying, perturbing the shape of the spheroid.

The viability of LAM spheroid cultures also decreased significantly following rapamycin treatment.

## DISCUSSION

In this study, we have designed a 3D spheroid model for LAM and examined its structure and drug response to rapamycin. Our next aim is to design a 3D vascularized LAM spheroid model that physiologically resembles the solid LAM tumor and search for early diagnostical biomarkers and investigate potential therapeutic targets.

# DESIGN AND IMPLEMENTATION OF A PENDULUM TEST USING X-IMU ACCELEROMETERS FOR QUANTITATIVE CHARACTERISATION OF MUSCLE SPASTICITY

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## INTRODUCTION

We investigated the spasticity of the musculus quadriceps using the X-IMU accelerometer. Spasticity is abnormal muscle tension caused by the muscle remaining in prolonged contraction. This phenomenon is caused by injuries of the central nervous system. To determine the presence and extent of spasticity, clinicians apply usually a subjective scale, the Modified Asworth Scale (MAS). Here we apply objective, quantitative assessment of spasticity.

## METHODS

We used an X-IMU accelerometer to define a measurement protocol that was tested on 10 neurologically intact able bodied persons. During the measurement, subjects sat on a table with the knee at the edge of the table and fully extended horizontally in a starting position. The accelerometer was placed over the lateral ankle and the acceleration along the x-axis tracked flexion-extension displacements of the knee joint after the leg was released. I connected the device to my laptop via bluetooth. The acceleration was recorded from the starting position, to the complete resting state, when the knee stopped at around 90° flexion.

## RESULTS

We evaluated the X-axis acceleration as a function of time, including the number of acceleration peaks in the extension direction, the durations between peaks, and the equation of the envelope curve fit to the recorded function. On average, we see 8.4 peaks, 2.04 s inter-peak duration, 3.229 m/s^2 first peak value and 19.89 s total decay time.

## DISCUSSION

The results of my subjects are in agreement with the literature results. The data processing should be tested with AI or classification algorithms to see if the whole measurement process can be automated. This would help the work of physiotherapists.

## ACKNOWLEDGMENT

Want to say thank you for the opportunity and work to my internal and external consultants.

# DEVELOPMENT OF OUR UV-INACTIVATION CHAMBER FOR SARS-COV-2: CHAMBER DESIGN AND UV REFLECTIVE MATERIALS

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## INTRODUCTION

Ultraviolet (UV) light inactivation is an effective method for the complete inactivation of viruses without damaging the protein structure of the pathogens. The efficiency of the inactivation depends on the overall dose of UV light (UV-C, 254nm). Light can reach the sample directly from the light source or via reflection on the chamber's inner coating. Depending on the material of choice, the dose delivered by reflected UV light can theoretically be up to 99%.
With our chamber's geometry and material usage, we standardize the inactivation of SARS-CoV-2 in an enclosed polypropylene Microcentrifuge (1.5ml) tube.

## METHODS

UV film dosimetry was used to establish the UV illumination profile. Reproducibility was demonstrated with multiple repeats of plaque assays at different UV doses and virus titers (virus titers were established in standard $TCID_{50}$/ml units for our virus stock).

## RESULTS

The dosimetric tests showed that only the side facing the UV light source is subjected to irradiation without reflectivity. Our setup's energy dosage from direct illumination is around 100 mJ/cm$^2$. Without reflection, we detected no sign of UV illumination on the back side of the microcentrifuge tube. Indirect illumination via reflection produced a roughly 25 mJ/cm$^2$ dose. Repeated cytopathic effect evaluations showed that our system is capable of the consistent, complete inactivation of SARS-CoV-2, Wuhan (virus titer = $6{,}31\times10^2$ $TCID_{50}$/ml) at 5 seconds irradiation. For a virus titer of $8{,}43\times10^5$ $TCID_{50}$/ml SARS-CoV-2, delta variant, 30-sec irradiation causes complete and uniform inactivation.

## DISCUSSION

Our system can reproducibly inactivate SARS-CoV-2 variants in enclosed microcentrifuge tubes. Our chamber geometry and reflective properties ensure that we can effectively irradiate the SARS-CoV-2 virus sample in volume. Further downstream use of the inactivated virus saves the research group and partners time and expenses.

## ACKNOWLEDGMENT

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# INDUCTION OF OSTEOGENESIS IN THE MG-63 HUMAN OSTEOSARCOMA CELL-LINE

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## INTRODUCTION

Induction of osteogenesis is a highly investigated field of regenerative medicine. The suitability of the osteogenic models to form bone-like structures is determined by the cell culture media applied during cell culturing. Additionally, cells grown in 2D or in 3D cell cultures show distinctively different expression levels of characteristic osteogenic differentiation markers. Our aim was to investigate the osteogenesis of MG-63 cells cultured in 2D monolayer cultures in contrast to 3D bioprinted models using GELMA bioink.

## METHODS

To investigate the mineralization of MG-63 human osteosarcoma cell line, 3D bioprinted models (BioX Bioprinter, GELMA Bioink, Cellink) were cultured for three weeks in □-MEM cell culture medium and compared to 2D monolayer cells cultured in DMEM or □-MEM cell culture medium. The mineralization of the MG-63 cell layers was visualized by Alizarin Red staining, using light microscopy. Gene expression of osteogenic markers was evaluated by TaqMan arrays.

## RESULTS

The results of Alizarin Red staining show an intense level of mineralization in 3D bioprinted MG-63 models after three weeks of incubation in □-MEM cell culture medium. Additionally, the detected gene expression changes can confirm the induction of osteogenesis. All five investigated osteogenic markers (Col1A1, BGLAP, BMP2, FN1, SP7) showed increased levels of gene expression in the 3D bioprinted MG-63 models after 3 three weeks of incubation in contrast to the 2D cultured MG-63 cell layers.

## DISCUSSION

The study shows significant differences in 2D cultured and 3D bioprinted MG-63 models. While in the 2D cultures the □-MEM medium induced only some osteogenic markers, in the 3D bioprinted model the level of all five osteogenic markers increased dramatically, indicating that the osteogenic differentiation was more successful in the bioprinted MG-63 cell system. Such models will make our further tissue differentiation studies and drug testing experiments possible.

# SURGAI – AUTOMATED ASSESSMENT IN LAPAROSCOPIC SURGERY EDUCATION

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## INTRODUCTION

Laparoscopic training is part of the medical education worldwide. Operating room training is extremely difficult due to time constraints, planning issues and ethical considerations. Therefore, it is a common practice to train novice surgeons on simulators. [1] Training requires an expert mentor but often there are a lack of them, and evaluate training sessions is time consuming. [2] Our aim is to automate the assessment of laparoscopic training session carry out in training boxes with AI based software.

## METHODS

We collected video records of laparoscopic training sessions from Semmelweis University. For education they used a training boxes and peg transfer exercise. The evaluation is based on the total duration of the session, the path of the instruments, and errors like drop of the sponge. We annotated the videos in CVAT, trained models with pytorch and measure distances with aruco markers.

## RESULTS

We could detect the different objects like the sponge, the instrument header, the spikes on the videoframes with 95% accuracy and sponge drop error with 89% accuracy. From the positions of the headers, we could calculate the movement and path length during the practice, and show the result in graphs. these measurements and session duration we could give an objective score from each practice.

## DISCUSSION

Based on our results an AI based automated assessment software for laparoscopic training seems to be achievable. As next steps we plan to widen the range of mistakes, and improve our model's accuracy.

## ACKNOWLEDGMENT

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# CREATING ARTIFICIAL BONE TISSUE USING 3D TISSUE PRINTING AND MESENCHYMAL STEM CELLS

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## INTRODUCTION

One of today's great challenges, not only in the clinical field but also in research and education, is the creation of human tissues and organs. This is particularly challenging for therapeutic purposes, due to the significant shortage of human tissue and organ donors. Therefore, in the last decades, research has been initiated to create artificial tissues and organs. Alongside cell and tissue culture, 3D tissue printing is the technology most capable of creating structures that resemble the structure and behavior of native tissues, especially at a scale relevant for implantation. Our goal was to create artificial bone tissue A) where we can use hydrogel in addition to the hard scaffold to allow cells to survive B) where the three-dimensional structure of the hard scaffold allows nutrients to enter the cells.

## METHODS

The 3D structure of the hard scaffold was created using Solid Edge Academic software. PCL was used as the model material of the hard scaffold, mimicking the artificial bone tissue. The two main components of the hydrogel were 10% GelMa and 2.5% alginate, which were mixed with AD-MSC. 3D constructs cultured in vitro after bioprinting and differentiated into bone. Constructs were printed using an Allevi 3D bioprinter. Optical and scanning electron microscopy were performed on the samples.

## RESULTS

Macroscopic morphological examination of the PCL scaffolds at double layer thickness showed that the scaffolds had the expected geometry, with pores well permeable in three orthogonal directions. The shape fidelity and dimensional accuracy were good, with no significant deformities or lesions. Scanning electron microscopy (SEM) confirmed this with few exceptions and provided additional information on the surface quality of the printed scaffold. AD-MSC cells survived bioprinting in the hydrogel. The cells were detectable either in aggregates, in groups or individually, throughout the hydrogel. Cell viability assays proved that the cells survived 3D tissue printing and exhibited a viability of over 90% 4 days after printing. Alizarin-red staining during bone directional differentiation revealed mineralization foci, which was positive in our case, after 7 days of differentiation. Calcium deposits formed by AD-MSC could be observed only in the hydrogel, with no evidence of differentiation or calcification in PCL.

## DISCUSSION

One of the main advantages of using hybrid 3D constructs, i.e. integrating rigid scaffolds and soft hydrogels is that the complete bioscaffold provides improved mechanical properties and a suitable biological microenvironment for the cells inside it. This also ensured the survival and differentiation of AD-MSC in our system. Considering that PCL is hydrophobic and hence has very limited cell adhesion, the use of hydrogel increased the biological functionality of the scaffold.

It is important to mention that most of the constructs we have prepared, and the results reported in the literature so far are small sized objects, which limits their clinical applicability.


## ACKNOWLEDGMENT

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# CHARACTERIZATION OF A THREE-DIMENSIONAL CORNEA MODEL

**Tamás Monostori[1,2], Melinda Guba[1,2], Diána Szűcs[1,2], Lajos Kemény[1,2], Zoltán Veréb[1,2,3*]**

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## INTRODUCTION

Corneal blindness due to infections, corneal dystrophy and other causes is a serious health problem worldwide. Even with a sufficient number of corneal donors, there is a significant demand for finding a properly transplanted cornea, this high demand is driving the creation of artificial corneal substitutes that must meet a number of criteria. Today, patient-specific treatment is becoming increasingly popular in modern medicine. Our aim was to create 3D constructs using corneal stromal-derived cells (CS-MSCs), an in vitro model that can be used to test drugs or perform regenerative medicine studies.

## METHODS

CS-MSC cells were used to create alginate-based spheroids (1x105 cells/spheroid). The morphology was monitored by microscopy for 28 days. The ultrastructure of the constructs was analysed by Transmission Electron Microscopy (TEM). Cell viability within the construct was determined by fluorescence microscopy. Morphology of construct was observed by histological staining.

## RESULTS

CS-MSCs were able to survive in 3D structures for 28 days. Viability did not change significantly; the external region was more viable than the inner one. Analysis of TEM images showed that the cells had active extracellular matrix production. However, due to the use of alginate, the cells were located in distinct niches as the histological staining showed.

## DISCUSSION

Alginate-based spheroid systems can be used to organize large numbers of cells into 3D structures and for long-term culture. However, alginate encapsulates the cells, so cell movement in the spheroid is limited. Further functional studies are planned to assess the immunological status of the cells.

## ACKNOWLEDGMENT

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# COMFORT PARAMETERS MEASURING IOT DEVICE FOR BASIC HUMAN HEALTH MONITORING IN OFFICE ENVIRONMENT

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## INTRODUCTION

In an office environment, the employees' satisfaction is based on personal comfort and health. Human comfort is mainly determined by temperature, humidity, light, and background noise. In the present research project, our aim is to develop a mobile IoT device to measure comfort-related quantities and display the data through cloud system. The resulting comfort parameters data would also be used for creating a thermal comfort map. Using this thermal comfort map, the employee can choose the most suitable workstation.

## METHODS

The device is based on ESP32 microcontroller, which is a cheap and powerful microcontroller for IoT applications. For the temperature and humidity, we used BME280 sensor. The ambient light sensor used is BH1750. KY-038 sensor is used to detect and measure ambient noise.

## RESULTS

We came to the conclusion that this device is needed in the indoor workspaces to monitor the comfort parameters ensuring a healthy and comfortable working environment.
Currently we have a prototype of the electronics and the design of the enclosure of the device including the placement of the sensors.

## DISCUSSION

We designed the device to get clear and accurate readings from four different sensors without interference in the data collected. For the enclosure, we designed it in such a way that it is flexible to be mounted on the wall, ceiling or table.

## ACKNOWLEDGMENT

This research is under the umbrella of "Parameterized Comfort in Physical Spaces" research group.

# 3D BIOPRINTING OF HUMAN PANCREAS CANCER MODEL

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## INTRODUCTION

Pancreatic tumor is the fourth cause of death among the deadliest malignancies. However, at diagnosis, <20% of patients have a resectable tumor. For better drug development and to provide personalized therapeutic options, models that more closely resemble native pancreatic tumors environment are needed instead of conventional monolayer cell cultures. We aimed to create 3D printed tissue-like construct of pancreatic tumor using the Capan-1 pancreatic cell line in Alg-GelMA scaffold.

## METHODS

Constructs were printed using an Allevi 3D bioprinter. Capan-1 cells were homogenized in 3% SA and 10% GelMA hydrogel at $5\times10^6$ cell/ml density. The 3D objects were created using Solid Edge Academic software. The Pneumatic extrusion 3D printer (Allevi3) is used for dispensing the bioink through a conical nozzle (D = 152 µm). SEM and confocal microscopy were performed on the samples. Live/dead staining used to evaluate viability of the cells. The cells morphology was monitored under Olympus high-throughput imaging system.

## RESULTS

Using the Allevi 3D bioprinter, we produced mesh-like constructs in which Capan-1 cells took on a 3D arrangement. The engineered tissues were kept in DMEM for 28 days. The proliferation rate was high and viability was more than 80%. The cells distinctly were colonized within the construct.

## DISCUSSION

3D tissue printing is appropriate method for the creation of artificial tumor tissue-like structures. In addition, we will investigate the effect of Oncotherapy drugs on the fabricated pancreatic tumour-like tissue.

## ACKNOWLEDGMENT

This work was supported by the National Research, Development and Innovation Office (NKFIH PD 132570 to ZV). ZV is a recipient of the János Bolyai Research Scholarship of the Hungarian Academy of Sciences (BO/00190/20/5) and the ÚNKP-21- 5 Bolyai+ Fellowship (ÚNKP-21-5 -SZTE-169) financed by the New National Excellence Program of the Hungarian Ministry for Innovation and Technology from the source of the National Research Development and Innovation Fund. Project no. TKP2021-EGA-28 and TKP2021-EGA-32 has been implemented with the support provided by the Ministry of Innovation and Technology of Hungary from the National Research, Development and Innovation Fund, financed under the TKP2021-EGA funding scheme. The funders had no role in study design, data collection, analysis, publishing decisions, or manuscript preparation.

# THE EFFECT OF SURFACE DISINFECTION ON MECHANICAL BEHAVIORS OF FLEXIBLE 3D PRINTED MATERIALS IN MEDICAL DEVICE DEVELOPMENT

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## INTRODUCTION

In many cases, 3D printing technologies have proven to have inimitable advantages in the development and production of medical devices. Surface disinfection always has taken on a prominent role in preventing the spread of infections. In this research, we have investigated the effects of different type of surface disinfectants on mechanical behavior and usability. Flexible materials were examined: our goal was to create proper disinfection recommendations for the available flexible 3D printing materials.

## METHODS

During the research, the test specimens were made with Stereolithography (SLA) and Fused Filament Fabrication (FFF) 3D printing technology with Thermoplastic elastomer (TPE). As an SLA technology the following materials were used: Elastic 50A and Flexible resin V2. The different disinfection methods have been compared with an untreated group, where disinfections were carried out with 70% Ethanol and Suma Tab D4 solution. The printed specimens were disinfected according to the manufacturers' procedures using these disinfection procedures. Every disinfectant method was repeated 5 times with 5 specimens. Tensile, Shore A hardness, compression, flex resistance and cross-section measurement tests were performed on all specimens 5 times according to ISO standards. The statistics have been carried out with two sample t-test.

## RESULTS

The values of Compression Young's modulus and Shore A hardness did not show any significant difference between untreated and disinfected specimens. The 2,000 cycles of the flex resistance test were endured by both the untreated and treated samples of TPE, though the crumpled surface became slightly polished. Flexible untreated specimens ruptured at cycle 63.6 ± 31.13 and the Elastic 50A untreated at cycle 91.2 ± 37.51. No significant changes occurred after the disinfection treatment. During the tensile tests, the Elastic 50A and TPU treated and untreated samples did not show any significant differences. The tensile strength of the samples of Flexible disinfected with Ethanol and Suma Tab D4 increased significantly compared to the untreated ones. The tensile strength of the untreated specimens was 2.02 MPa ± 0.25 MPa, 3.44 MPa ± 0.51 MPa with ethanol and 2.62 MPa ± 0.31 MPa with Suma Tab D4 disinfection. During the cross-section test, the Flexible and TPE samples treated with ethanol and the Elastic samples treated with Suma Tab D4 show a significant change compared to the untreated ones.

## DISCUSSION

Tests have proven that the elastic and TPE materials are resistant to various surface disinfections. With regard to the Flexible material, the change in tensile strength must be taken into account. Flexible and Elastic are great to increase comfortability for users. The examined materials are excellent for making devices that could be used in the clinic, such as sanitation kits, ventilator connectors, ECG limb lead connectors.

## ACKNOWLEDGMENT

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# SUSTAINABLE USING OF WASTE MATERIALS IN CONCRETE

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## INTRODUCTION

Concrete is the most often used building material in the world. As a result, the mass extraction of raw resources necessary for concrete production has significant environmental effects. Every year, over ten billion tons of concrete are produced, resulting in the depletion of natural resources and a large carbon dioxide emission. One of the key aims of concrete technology nowadays is to minimize the usage of Portland cement and natural fine aggregates by partially substituting waste materials and by-products of industrial activities.

## METHODS

In this study, the issues of economic and environmental concerns are ad-dressed by using glass waste, silica fume, and steel slag aggregate as a partial replacement for fine aggregates and cement in concrete. Moreover, this research analyzes the impacts of using recycled tire steel fiber in concrete on the tensile characteristics of concrete

## RESULTS

The results of the tests revealed that the use of steel slag aggregates and silica fume may enhance the compressive strength of normal concrete and can be effectively utilized to produce normal grade concrete. Glass waste is primarily suggested for lower grade concrete mixtures. The results support the potential usage of recycled fibers in producing environmentally friendly fiber reinforced concrete. However, it has been shown that the performance can be improved further by removing the attached rubber from the recycled fibers

## DISCUSSION

Test results confirmed that the use of steel slag aggregates and the silica fume can increase compressive strength of normal concrete and can successfully be used for the production of normal grade concrete glass waste is mainly recommended for lower grade concrete mixes The findings suggest the use of recycled fibers in the production of ecologically friendly fiber reinforced concrete.

## ACKNOWLEDGMENT

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# TOWARDS BETTER DRUG DEVELOPMENT – 3D MODEL FOR TOXICOLOGY RESEARCH

**Diána Szűcs[1,2,3], Zsolt Fekete[4], Melinda Guba[1,3], Tamás Monostori[1,3], Lajos Kemény[1,3], Katalin Jemnitz[4], Emese Kis[4], Zoltán Veréb[1,3,5*]**

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## INTRODUCTION

Metabolism and toxicology studies on liver cells are of paramount importance in drug development. However, conventional monolayer liver cell cultures have several limitations in classical measurements. They are not suitable for long-term measurements and do not fully reflect the environment of the liver as a tissue. Our aim was to maintain liver cells in a 3D structure that better models the native environment and to test their suitability for toxicological studies.

## METHODS

We created alginate-based 3D spheroid systems using HepG2 cells. The spheroids contained between 50,000 and 100,000 cells. The spheroids were cultured for 28 days and their morphology was monitored by microscopy and TEM measurements. Cell viability was detected by LIVE/Dead staining. For the toxicological measurements, gene expression of CYP enzymes involved in drug metabolism was assessed by RT-PCR.

## RESULTS

The 3D spheroids were maintained in vitro for 28 days. Cell viability remained stable for 28 days and cell ultrastructure showed active protein synthesis. Studying CYP450 expression and the enzyme induction potential, cells were treated with Omeprazole, Flumazenil, Phenobarbital, Rifampicin, CITCO and Chlorpromazine. Gene expression analysis demonstrated elevated expression of CYP1A2 by Omeprazole, CYP2B6 by CITCO, CYP3A4 by Rifampicin compared to the untreated control.

## DISCUSSION

These experiments prove that 3D spheroid systems, from HepG2 cells, are suitable for the long-term maintenance of liver cells, enabling the performance of viability and toxicological studies based on the CYP expression pattern.

## ACKNOWLEDGMENT

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# HEMOKININ-1-INDUCED TRANSCRIPTOMIC ALTERATIONS IN RAT TRIGEMINAL GANGLION PRIMARY SENSORY NEURONS RELATED TO PAIN SIGNALLING

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## INTRODUCTION

Hemokinin-1 (HK-1) is a neuropeptide inducing a variety of processes involved in pain and inflammation, but its precise roles still remain unclear. Classic receptors of HK-1 are neurokinin receptors NK1, NK2 and NK3; however Mas related G protein receptors (Mrgprs) were also described as potential targets. Recently, our data demonstrated NK1R-independent calcium influx in rat cultured trigeminal ganglion (TRG) cells induced by 1 μM, but not 500 nM HK-1 [1]. Here we used a transcriptomic approach to investigate the intracellular mechanisms and signalling pathways exerted by these HK-1 concentrations in order to explore its mechanism of action in TRG primary sensory neurons.

## METHODS

Samples were collected 6h and 24h after HK-1 treatments. QuantSeq 3' mRNA-Seq Library Prep Kit FWD for Illumina and TapeStation 4200 were used. Sequencing was performed on the Illumina NextSeq550 platform to produce 75 bp single end reads. Read alignment with STAR v2.5.3a, followed by reads association using HTSeq library v0.11.1 were done. Gene count data were normalized using the trimmed mean of M values (TMM) normalization method of the edgeR R/Bioconductor package. Data were further log transformed using the voom approach for statistical evaluation in the limma package. Fold change (FC) values between the compared groups resulting from linear model fitting and modified t-test p-values were calculated by the limma package [2].

## RESULTS

The tachykinin NK1 or NK2 receptors were not detected in the cultures. Differentially expressed (DE) genes were determined by filtering thresholds. All treatments resulted in numerous DE genes in TRG cells compared to the untreated group (1 μM 6h: 140; 500nM 6h:100; 1μM 24h: 175; 500 nM 24h: 351). Notable DE genes include ANTXR2 (Anthrax toxin receptor 2) and PAR-1 (Proteinase activated receptor-1). Enrichment analysis of DE genes was performed using the KEGG (Kyoto Encylopedia of Genes and Genomes), GO (Gene Ontology) and Reactome databases. Calcium signalling was implicated as one of the enriched KEGG pathways (G alpha (s) signalling events, Opioid Signalling from Reactome and protein kinase A inhibitory activity GO term (1 μM 6h). Postsynaptic neurotransmitter receptor activity, citokin activity were found significant GO term (1 μM 24h) as well, in contrast to the 500 nM treatment.

## CONCLUSION

Our analysis highlights concentration- and calcium influx-dependent effects of HK-1 related to pain processes in primary sensory neurons, which are independent of the NK receptors.

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# TOWARDS BETTER DRUG DEVELOPMENT – 3D MODEL FOR TOXICOLOGY RESEARCH

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## INTRODUCTION

Metabolism and toxicology studies on liver cells are of paramount importance in drug development. However, conventional monolayer liver cell cultures have several limitations in classical measurements. They are not suitable for long-term measurements and do not fully reflect the environment of the liver as a tissue. Our aim was to maintain liver cells in a 3D structure that better models the native environment and to test their suitability for toxicological studies.

## METHODS

We created alginate-based 3D spheroid systems using HepG2 cells. The spheroids contained between 50,000 and 100,000 cells. The spheroids were cultured for 28 days and their morphology was monitored by microscopy and TEM measurements. Cell viability was detected by LIVE/Dead staining. For the toxicological measurements, gene expression of CYP enzymes involved in drug metabolism was assessed by RT-PCR.

## RESULTS

The 3D spheroids were maintained in vitro for 28 days. Cell viability remained stable for 28 days and cell ultrastructure showed active protein synthesis. Studying CYP450 expression and the enzyme induction potential, cells were treated with Omeprazole, Flumazenil, Phenobarbital, Rifampicin, CITCO and Chlorpromazine. Gene expression analysis demonstrated elevated expression of CYP1A2 by Omeprazole, CYP2B6 by CITCO, CYP3A4 by Rifampicin compared to the untreated control.

## DISCUSSION

These experiments prove that 3D spheroid systems, from HepG2 cells, are suitable for the long-term maintenance of liver cells, enabling the performance of viability and toxicological studies based on the CYP expression pattern.

## ACKNOWLEDGMENT

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# 3D MICROTUMOURS BY MICROFLUIDICS: FABRICATION AND APPLICATIONS

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## INTRODUCTION

Conventional two-dimensional (2D) cell culture is well-established but suffers from disadvantages, such as limited cell-cell and cell-extracellular matrix interactions, resulting in cell flattening or cell remodelling.[1] Three-dimensional (3D) culture offers a more physiologically relevant tissue model.[2, 3]

## METHODS

We have fabricated 3D microtumours (3D-MMT) by a microfluidic technique in which tumour cells are encapsulated in viscous gels (e.g. Matrigel, collagen, agarose). In an example application, 3D-MMTs containing ovarian cancer cells were treated with first-line chemotherapeutics (carboplatin, paclitaxel). Cells remaining after chemotherapy, minimal residual disease (MRD), can reinitiate the tumour growth.[4] RNAseq analysis was performed to validate 3D-MMTs in MRD study.

## RESULTS

~100 3D-MMTs, of uniform-size and -composition, can be prepared in just 3 minutes. The diameter of the 3D-MMTs can be adjusted (300 to 900 μm), various shapes can be prepared (sphere, ellipsoid), and the cellular contents can be controlled. The 3D-MMTs can be cultured for up to 8 weeks.
3D-MMTs exhibited EC50 values of 97.5 ± 8.1 μM (carboplatin) and 10.3 ± 3.0 nM (paclitaxel), which are higher than 58.4 ± 3.5 μM (carboplatin) and 3.7 ± 1.7 nM (paclitaxel) for 2D cultures.
RNAseq analysis demonstrated that MRD 3D-MMTs recapitulated all 5 gene signatures found in samples from patients, while only one signature was present in 2D-cultured MRD cells. Further, a cytotoxicity assay showed that MRD 3D-MMTs are more sensitive to fatty acid oxidation inhibitors than treatment-naïve 3D-MMTs.

## DISCUSSION

Batches of hundreds of 3D-MMTs can be generated, and can be used as a realistic model for rapid drug screening. The 3D-MMTs offered higher drug resistance than 2D cultures. RNAseq results revealed that 3D-MMTs recapitulate in vivo tissues better than 2D cultures.

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# LOAD CAPACITY TEST OF 3D PRINTED MYOELECTRIC PROSTHETICS

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## INTRODUCTION

In response to the need for accessible prosthetics, the University of Pécs has developed “Ember Arm”, which is a 3D printed myoelectric hand capable of performing different types of grips used commonly in daily activities such as to hold a glass of water, sign with a pen, make a sandwich, which sounds really easy and actually, most of us perform a lot of these tasks automatically without even noticing. In any case, for people with amputations or malformations in their upper limbs, those simple tasks could become the most difficult part of the day. My research is about performing different tests of fatigue and durability in order to know how long the Ember Arm can last if a person uses it in his/her daily activities. Since the prosthetic hand was printed in a polymer material and even when 3D printing technology have changed the perception of health and medical systems, it is hard to tell the effectiveness of such stuff. That is why is very important to perform these reliability tests.

## METHODS

In order to know the durability of the prosthetic hand is necessary to perform two different types of tests:

**Fatigue test.** – For this test, a universal material tester machine is used. With this machine, is possible to determine the resistance in the fingers of the prostheses until fatigue occurs. In order to determine the fatigue in the fingers is necessary to design fixation components and place them between the parts of the fingers and the tester machine. After the proper measurements and data acquisition with the machine, is necessary to perform the data analysis and statistics. In this way is possible to determine how long the prostheses can last before failure, which is the purpose of this research.

**Finger durability test.** – Apply a cyclic flexo- extension test to measure the endurance of a finger under the application of several fatigue cycles and to determine the mode of failure under this condition to verify the damage in the joints and the components.

## RESULTS

The research is being developed, its completion is scheduled for June 2023.

## DISCUSSION

This research will impact many people´s lives since we will have an approximation of the life of the prosthesis before it fails. In that way the physician and the person using it can be aware about when it is time to replace or do maintenance of the upper limb prostheses.

# ONLINE

PRESENTATIONS

# INFLUENCE OF THE APPLIED 3D PRINTING METHODOLOGY ON THE POLYAMIDE SAMPLES MECHANICAL PROPERTIES

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## INTRODUCTION

Due to the wide range of possibilities of 3D printing technology and materials, additive methods are increasingly used in the medical industry. One of the materials used is Polyamide 12 (PA 12) - a biocompatible material with excellent physical properties, characterized by high mechanical strength and low water absorption value [1,2].

The aim of the work was to determine the mechanical properties of nylon samples printed with the use of two different additive technologies consisting in extrusion of semi-fluid material (FDM) and selective laser sintering (SLS).

The scope of my work included printing samples from PA 12, subjecting them to a uniaxial compression test and, on the basis of the obtained results, determination of the strength parameters of the tested material.

## METHODS

The research began with the creation of virtual, cylindrical 3D models. Then, using SLS and FDM methods, respectively 120 and 104 samples of three different (3, 6 and 9 mm) diameters and five different angles (0, 30, 45, 60, 90 °) of inclination were printed.

The samples were cleaned, carefully measured, and then subjected to uniaxial compression test on the MTS 858 Mini Bionix testing machine. The data obtained from the device allowed to determine the compressive strength, Young's Modulus and stiffness for the tested samples. From the compilation of the individual results, a statistical analysis was performed.

## RESULTS

The diameters, the angle of inclination and the printing method of the samples influenced the obtained strength parameters.

The obtained strength values of samples with diameters of 6 and 9 mm were on average 50% higher than in the case of elements with a diameter of 3 mm. Samples obtained with the SLS method were characterized by better mechanical properties than those obtained with the FDM technology. For SLS and FDM printing technology, samples printed at 0 and 90 ° were characterized by the best strength properties.

## DISCUSSION

I come to the conclusion, in order to obtain the most durable elements, they should be printed in a larger size, using the SLS method, positioned vertically or horizontally in relation to the build plate.

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# ANALYSIS OF THE INFLUENCE OF INTELLECTUAL EFFORT ON THE BASIC WAVES AND RHYTHMS OF THE EEG SIGNAL

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## INTRODUCTION

Electroencephalography (EEG) is a test designed to record the bioelectrical activity of the brain and enable the assessment of the work of the central nervous system. It is very useful in the diagnosis of diseases from the group of epilepsy, brain tumors, sleep disorders, as well as in determining the type of coma. During the test, a signal is recorded, from which several basic waves can be distinguished: alpha, beta, delta, theta and gamma. The waves differ in frequencies and amplitudes.

This work aimed to determine the effect of type of intellectual effort based on the main waves and rhythms recorded during EEG examination.

## METHODS

Firstly, the applications of EEG testing were reviewed. Next, a study design was established, with each individual part designed to simulate one type of intellectual effort. During the successive stages, the participant had to solve tasks in history, mathematics, spelling, English, and recognition of objects in a picture in a puzzle form. All parts of the test were conducted in such a way as to exclude as far as possible any interference in the recorded signal caused by movement or speaking of the subject. The signal was recorded using a BIOPAC MP35.9 device and ECG EK-S 50 PSG medical electrodes.

The study involved fourteen people, including seven men and seven women. The tests were held in a quiet room, and were conducted in such a way as to exclude as far as possible any interference in the recorded signal caused by movement or speaking of the subject.

## RESULTS

During the analysis, two pairs of subjects were compared: two 21-year-olds who were in the process of technical studies and two subjects over 55 years old, one with a technical education and the other with a humanistic education. The analysis includes calculation of the mean standard deviations, and the average frequencies for each rhythm during each part of the tests.

## DISCUSSION

During the analysis of the test results, it was found that the differences between individuals can be very clear, even in the case of a reference signal that was not influenced by the knowledge of the subject. In the case of the younger pair, less frequent occurrence of large differences between the frequency ranges defined by the standard and the results obtained during the tests was observed.

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# iCBEI

ABSTRACT BOOK