The Faculty of Biomedical Engineering
Technion

Projects Conference
June 16th, 2016

Abstracts

הטכניון
מכון טכנולוגי
לישראל

Dear all,

The Annual Projects Conference in Biomedical Engineering is hosted by the department of Biomedical Engineering at the Technion – Israel Institute of Technology. As the dean of the Biomedical Engineering department and as the project course staff, we are pleased and honored to welcome you here.

The conference is hosting 4th year students who are eager to present their year-long projects and to receive feedback from academic researchers, industrial experts, and their peers. These projects implement the medical, engineering, and scientific tools that the students have acquired and developed during their BSc journey in Biomedical Engineering.

The students aim to provide solutions that meet research and development needs in the Biomedical industries and research departments. Through working on their projects, students gained invaluable, hands-on experience. They had to work through technical challenges and adhere to strict standards comparable to those in a real-world setting. We believe that this hands-on experience engages graduates with the Biomedical industry and/or the wide variety of Biomedical research in a very strong way encouraging multidisciplinary work that is vital to the students' futures.

Additionally, we encourage the students to think out of the box to initiate new solutions and help foster their entrepreneurship skills. Above all, these projects are a key element of the faculty vision which strives to strengthen the long-term cooperation between academia and industry leaders.

In this booklet we are introducing the abstracts of all presented projects. We wish all students rewarding careers and bright futures. We hope that one day they will take an active part in similar projects as professional mentors from both the industry and academia.

Kindest Regards,
Prof. Amir Landesberg, Faculty dean
Dr. Alex Vilensky, Course Instructor
Course TA: Ms. Hanan Khamis, Ms. Nasma Mazzawi and Dr. Oscar Lichtenstein

List of Abstracts

1 **Analyzing And Comparing Flow Regimes In Different Designs Of Glaucoma Shunts Using A Simple Flow System Device**

Harel Shani[1], Nitzan Pruschy[1], Alex Vilensky[1], Omri Caspi[2]
[1]Department of Biomedical Engineering, Technion - IIT, Haifa, Israel
[2]Hanita Lenses , Kibbutz Hanita ,Israel

2 **Engineering a Vascularized Muscle Tissue Graft In Vitro using Murine Cell Cultures**

Maria Elishaev[1], Alex Vilensky[1], Luba Perry[1]
[1]Department of Biomedical Engineering, Technion - IIT, Haifa, Israel

3 **Microfluidic Droplet Based System for Templated Nano-particle Aggregate Production**

Safaa Abdallah[1], Netanel Korin[1], Nasma Mazzawi[1], Maria Khoury Salameh[1]
[1]Faculty of Biomedical Engineering, Technion-IIT, Haifa, Israel

4 **Echocardiogram View Classification Utilizing Computer Vision Algorithms**

Roie Cohen[1], Grigoriy Zurakhov[1], Nasma Mazzawi[1], Hanan Khamis[1]
[1] Department of Biomedical Engineering, Technion - IIT, Haifa, Israel

5 **Interference of Existing Memories Through Reactivation Process of Visual Perception**

Yehuda Zur[1], Hanan Khamis[1] and Nitzan Censor[2]
[1] Department of Biomedical Engineering, Technion - IIT, Haifa, Israel
[2] School of Psychological Sciences and Sagol School of Neuroscience, Tel Aviv University, Tel Aviv 69978, Israel

6 **Acoustic Characteristics of the Thoracic Diaphragm for Focused Ultrasound Treatment of the Liver**

Roana Schiopu[1], Limor Arbel[1], Hanan Khamis[1], Lilach Shay[2]
[1] Department of Biomedical Engineering, Technion - IIT, Haifa, Israel
[2] InSightec Ltd, Tirat Carmel, Israel

7 **Early Assessment of Heart Function from Mitral Annulus Plane Excursion (MAPE) Semi-automatic Tracking**

Hadas Avraham[1], Uri Goldsztejn[1], Grigoriy Zurakhov[1], Hanan Khamis[1], Zvi Friedman[1, 2]
[1]Department of Biomedical Engineering, Technion - IIT, Haifa, Israel
[2]General Electric: Healthcare, Tirat Hacarmel, Israel

8 **Sensory Feedback – Raptor Reloaded**

Yair Herbst[1], Moran Davoodi[1], Oscar Lichtenstein[1], Yoav Medan[1,2]
[1] Department of Biomedical Engineering, Technion - IIT, Haifa, Israel
[2] Haifa3D Organization, Haifa, Israel

9 **Characterization of Mechanical Properties of the Hydrogels under the Different Values of Applied Physiological Stress**

Ekaterina Gurevich[1], Yael Diamant[1], Yulia Merkher[1], Oscar Lichtenstein[1], Daphne Weihs[1]
[1]Department of Biomedical Engineering, Technion - IIT, Haifa, Israel

10 Development of Applicative Methods for Reliable Portable and Real Time Control of 3D Printed Hand Prosthesis Using Surface EMG Signals

Aviv Peleg[1], Or Dicker[2], Oscar Lichtenstein[1], Tal Shnitzer[2]
[1]Faculty of Biomedical Engineering, Technion - IIT, Haifa, Israel
[2]Faculty of Electrical Engineering, Technion - IIT, Haifa, Israel

11 Enzyme-Based Bioreactors: Therapeutic and Industrial Applications

Tamara Shor[1], Adina Shatz[1], Yathreb Assad[1], Nasma Mazzawi[1], Daphne Weihs[1], Noah Lotan[1]
[1]Department of Biomedical Engineering, Technion - IIT, Haifa, Israel

12 A 3D Amplification Model of Pericytes for Muscle Tissue Regeneration

Avi Izraeli[1], Yair Hochner[1], Nasma Mazzawi[1], Olga Kossover[1]
[1]Department of Biomedical Engineering, Technion - IIT, Haifa, Israel

13 Implementation of 8 MeV Total Skin Electron Irradiation Based on the Stanford Technique

Reut Guy[1], Chen Avraham[1], Alex Vilensky[1], Shahar Daniel[2]
[1]Department of Biomedical Engineering, Technion - IIT, Haifa, Israel
[2]Department of Radiation Oncology, Rambam Health Care Campus, Haifa, Israel

(1)

Analyzing and Comparing Flow Regimes in Different Designs of Glaucoma Shunts Using a Simple Flow System Device

Harel Shani[1], Nitzan Pruschy[1], Alex Vilensky[1], Omri Caspi[2]

[1]Department of Biomedical Engineering, Technion - IIT, Haifa, Israel
[2]Hanita Lenses, Kibbutz Hanita, Israel

Introduction: Glaucoma is an eye disease afflicts millions of people worldwide. Glaucoma usually accompanied by increased ocular pressure (IOP) that gradually damage the optic nerve which leads to the deterioration of the peripheral vision , and may even lead to total blindness . IOP usually appears due to impaired drainage of the Aqueous Humour (i.e the fluid inside the eye's anterior and posterior chambers)

One common way to treat Glaucoma is transplanting a drainage device which controls the eye pressure. In practice 20 percent of all procedures end with complications and the quest for ideal shunt design is ongoing. Seeking a design that could increase the transplantation procedure success rates, "Hanita Lenses" developed some different Glaucoma shunt devices. In order to compare between the different designs we analyzed the flow regimes inside the shunts. By creating a simple, replicable and easy to use flow system device, that achieves minimal leakage, we were able to reach our goals.

Methods: We analyzed 3 different designs (figure 1), 5 implants from each design. In order to imitate the Aqueous Humor we used double distilled water which has similar properties. To achieve the desired physiological flow rate (i.e. 2.5 microliters per minute) we created a leak free flow system device connected to a simple syringe pump.

We added 3.2 micrometer fluorescent beads and used a binocular fluorescent microscope equipped with a camera in order to record the flow. The acquired data was analyzed using particle image velocimetry (PIV) software (DaVis High Speed and Matlab Piv Tool Box).From the analyzed data we were able to extract the velocity flow fields and the streamlines inside the shunts (figure 1). Finally we compared our empirical data with numerical results obtained initially using Solidworks software.

Results: By comparing the velocity vector fields at 9 points of interest, we could not statistically indicate significant difference of velocities between the 3 designs. On the other hand we did notice different streamlines which implies that the structure of design 12 is more hydrodynamic (figure 1).

Conclusions: Design 12 seems as the preferable design but in order to get a conclusive result farther evaluation should be obtained.

Keywords: Glaucoma, glaucoma shunt, flow regime, vector field, streamlines.

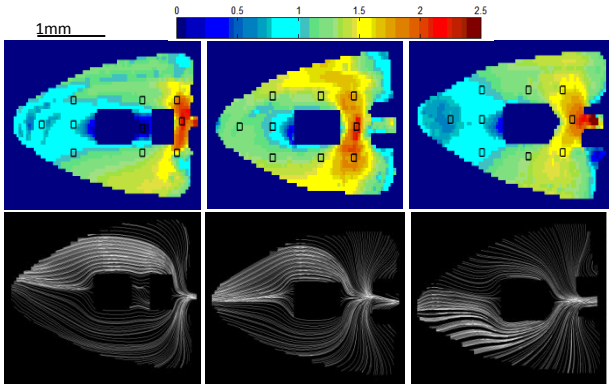

Figure 1: upper view of design 9, design 11, and design 12 (left to right). Upper figure: velocity field analysis (logarithmic scale [micrometer/sec]). Points of interest marked in black. Lower figure: stream line analysis.

(2)

Engineering a Vascularized Muscle Tissue Graft in vitro using Murine Cell Cultures

Maria Elishaev[1], Luba Perry[1], Alex Vilensky[1], Shulamit Levenberg[1]

[1]Department of Biomedical Engineering, Technion - IIT, Haifa, Israel

Introduction: The growth of new blood vessels inside implanted tissues and the connection of in-vitro grown blood vessels with those of the patient's body are the most important factors in tissue engineering success. This process is especially important in tissues with high oxygen consumption, and a muscle tissue is one of them. Previous studies showed advantages of using a tri-culture of endothelial cells (EC), fibroblasts and muscle cells (MC) in the engineering of vascularized muscle grafts. Seeding these types of cells together and growing them on a 3D scaffold *in-vitro* result in the formation of vascular networks inside the muscle graft and their rapid anastomosis with the host's blood system after implantation. EC and fibroblasts used in previous studies were of human origin, therefore, *in vivo* studies could be only done in nude mice, and immune response after implantations was not observed. In the present study, we used tri-culture of murine microvascular EC with satellite cells (SC) and fibroblasts extracted from mice limb muscles. We tried to find the optimal conditions for muscle graft growing and to determine for the first time if the using of murine cells is as effective in the formation of vessel-like networks as the using of human cells.

Methods: We used 3D synthetic biodegradable scaffolds from Poly lactic acid (PLLA) and Poly lactic co glycolic acid (PLGA) which simulate the mechanical properties of the tissue. Combinations of cells were seeded upon the scaffolds and after two weeks vessel-like networks were characterized according to their density, length and complexity.

Results: It was found that tri-culture of murine cells form 3D hollow vessels, which are different from the vessels seen in previous studies. It was also shown that SC presence does not disturb vessels formation, even in high concentrations.

Conclusions: The significance of this study is great: new vascularized muscle grafts can be transplanted into mice with functioning immune system, so both anastomosis and immune response can be studied. All types of cells can be extracted from biopsy of the patient; in regenerative medicine, using autologous cells can help to solve the problems of graft rejection by the patient's immune system and of the lack of donors. Our study is a step towards better understanding of vascularization of engineered grafts *in-vitro*, and towards future studies of anastomosis *in vivo*, after implantation into a host with an active immune system.

Keywords: Tissue Engineering, Muscle Tissue, Vascularization of Graft, Murine Cell Culture

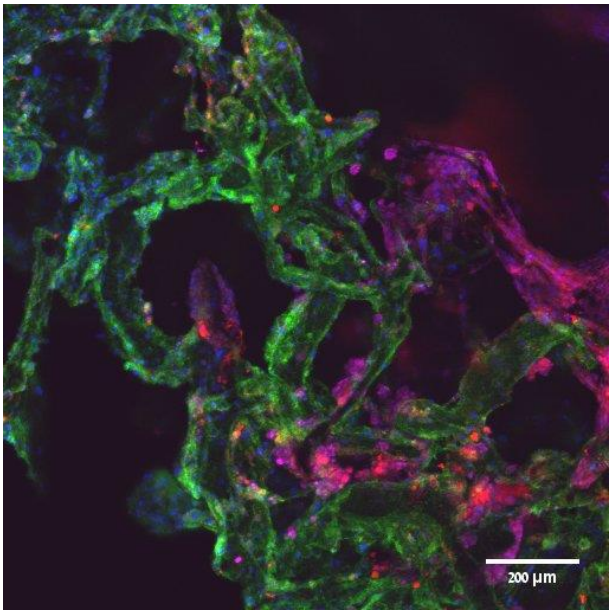

Figure 1: (x5 magnification) Vessel-like networks formatted in a scaffold 2 weeks after cell seeding. Immunostaining: EC – CD31 (green), SC – Desmin (pink), nuclear staining – DAPI (blue).

(3)

Microfluidic Droplet Based System for Templated Nano-particle Aggregate Production

Safaa Abdallah[1], Netanel Korin[1], Maria Khoury-Salameh[1]

[1]Faculty of Biomedical Engineering, Technion-IIT, Haifa, Israel

Introduction: Targeted drug delivery offers improved therapeutics by localizing the drug at the desired site thus increasing the drug efficacy and reducing its possible side effects. In this context, a variety of nanoparticle base drug carriers have been developed including nanoparticle aggregates. Nanoparticle aggregates are composed of a large number of drug-carrying nanoparticles inter-connected to each other and designed to breakup to their nanoparticle components at the desired site upon a stimuli. There are a few suggested methods to manufacturing these aggregates. The most common fabrication method is using spray drying. Unfortunately, these methods are based on expensive equipment, produce non-uniform aggregates and usually involve exposure to high temperature which could damage the drugs. In this project we propose to examine the use of a droplet microfluidics device to produce mono-dispersed nano-particle aggregates. The first step required to achieve this goal is to produce controlled, mono-dispersed water droplets using a droplet microfluidic systems.

Methods: Microfluidic droplet generators produce droplets by combining two or more streams of immiscible fluids and generating a shear force on the discontinuous phase causing it to break up into discrete droplets. In this study, a focused-Flow Droplet Generator chip was used to produce droplets (Fig 1), where two immiscible fluid streams shear the discontinued phase and produce droplets. We used water as the discontinued phase (droplet phase) and canola oil as the immiscible phase. Tween 20 was used as surfactant to reduce the surface tension between the two phases. All fluid were filtered through 0.2 micron filter prior to infusion. We examined two perfusion systems: 1) Flow rate based perfusion using syringe pumps 2) pressure controlled perfusion using a programmable commercial Fluigent ® system.

Results: Syringe pump based droplet production showed instabilities in the flow and are less suitable for droplet production. Pressure based perfusion, using the Fluigent system, showed stable flow in the system. However, higher flow rates than the current output pressure (<345mBar) are needed to produce droplet of defined sizes. The use of surfactant (Tween20) was critical in order to produce droplets. High flow rates (>100ul/min) are needed to remove bubbles from the systems prior to infusion of the fluids.

Conclusion: A system based on Focused-Flow Droplet Generator Chips using a pressure controlled infusion system, producing the required pressure gradient, is preferable for stable

droplet production compared to syringe based perfusion systems. Stable droplet production requires an optimized procedure in order to remove bubbles from the system and allow stable flow to form in the system.

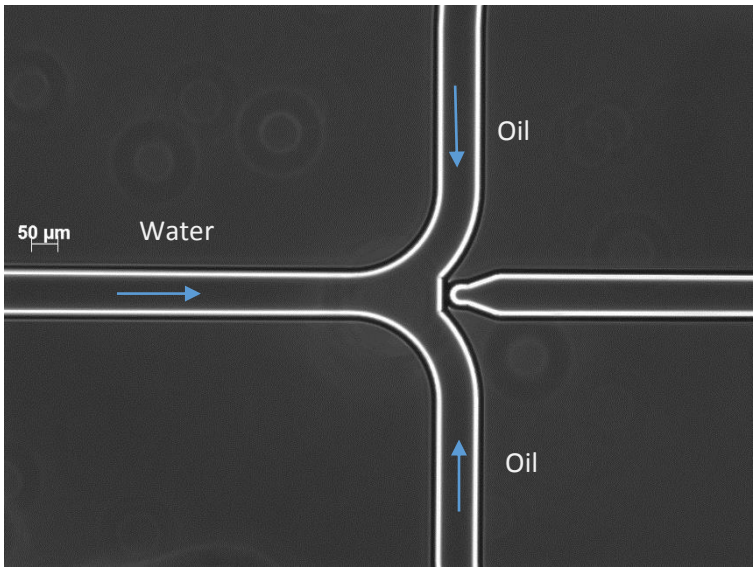

Figure1: A focused-Flow Droplet Generator chip.

(4)

Echocardiogram View Classification Utilizing Computer Vision Algorithms

Roie Cohen[1], Grigoriy Zurakhov[1], Nasma Mazzawi[1], Hanan Khamis[1]

[1] Department of Biomedical Engineering, Technion - IIT, Haifa, Israel

Introduction: Echocardiogram is one of the most routinely used imaging modality in cardiology due to its ability to allow non-invasive, time and cost-effective diagnostic tests with no radiation exposure compared to other imaging techniques. Currently there are various attempts to introduce novel methods for accurate and fast computer aided diagnosis, providing physician essential clinical markers to enhance immediate decision making.

A routine echocardiogram test includes imaging of different long and short axis views. Since a fast and accurate diagnosis demands fully automatic algorithms, an automatic classification of long and short axis views is required to begin with. Here we propose multi computer vision based approaches for view classification: a. 1st stage classification into long and short axis views, and b. 2nd stage classification into sub-views of the short axis view (Mitral Valve (MV), Papillary Muscles (PM) and Apex (AP)).

Methods: Two algorithms were adapted: the first algorithm is a machine learning method based on "LC-KSVD" which uses sparse representation of the data to learn a dictionary which enables to represent uniquely the data and classify it into the different classes. Dictionary training was performed using 70% of each class while the remaining 30% were used as test set. Only one downsampled frame per clip was selected at 250ms post R peak. The second method is based on the fact that the myocardial wall and the interventricular septum are strong ultrasonic reflectors which imply a strong correlation between the anatomy and the grayscale intensity of the image. A vertical summation of a 'Maximum Intensity Projection' (MIP) image created from 10 frames starting at 250ms post R peak. Then, the resulted 1D-vector was used as a unique parameter for classification.

A total number of 3452 clips/images was acquired during a routine echocardiogram test: long axis views (1053 clips), short axis views (452 clips), Doppler (747 images/clips, B-mode images (230 images) and others (518 images/clips). In addition, the short axis is composed of 109 clips of MV, 220 clips of PM and 123 clips of AP.

Results: The LC-KSVD algorithm yielded a success rate of 98% when used for the 1st stage classification. This algorithm yielded a success rate of 50% when applied for the 2nd stage classification of Short Axis View.

The MIP method yielded a success rate of 90% when used for 1st stage classification. This method was unable to achieve satisfying results for the 2nd stage classification, however, it has a great potential as an image quality index that is used as a pre-classification input to exclude undefined images.

Conclusions: Short/Long axis views have a unique grayscale pattern which could be used to distinguish between them. The LC-KSVD algorithm has shown a great potential as a 1st stage classification method. The dictionary used in the LC-KSVD approach requires a large data set in order to achieve high classification accuracy. Classification based on a single frame is sufficient for 1st stage classification, however it is insufficient for a 2nd stage classification. Motion detection based approaches will be considered for future work.

Keywords: Echocardiography classification, Computer Aided Diagnosis, Computer Vision, view classification

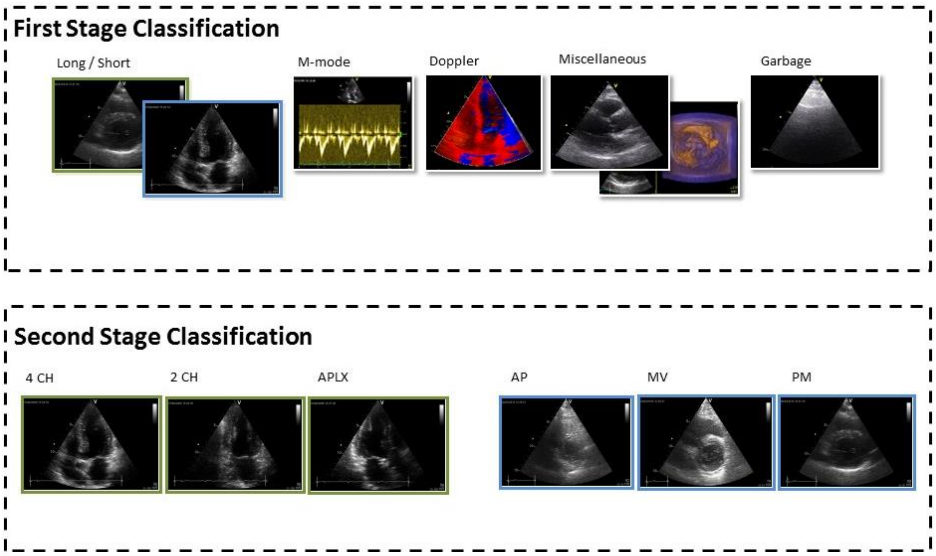

Figure 1 – An illustration of the different stages for classification

(5)

Interference of Existing Memories through reactivation process of visual perception

Yehuda Zur[1], Hanan Khamis[1] and Nitzan Censor[2]

[1]Department of Biomedical Engineering, Technion - IIT, Haifa, Israel

[2]School of Psychological Sciences and Sagol School of Neuroscience, Tel Aviv University, Tel Aviv, Israel

Introduction: Human perception thresholds can improve through perceptual learning processes for some simple visual discrimination tasks. Studies at the synaptic level, predominantly using Pavlovian fear conditioning paradigms in animal models, have shown that once an existing memory is reactivated it becomes susceptible to modulations. Studies have also shown that short reactivation processes are sufficient enough to induce offline gains and performance in visual discrimination tasks. Here, using a combination of behavioral, brain stimulation, and neuroimaging paradigms, we tested whether noninvasive repetitive transcranial magnetic stimulation (rTMS) interference to the primary visual cortical (V1) area following reactivation of visual memory reduces threshold improvement compared to control vertex stimulation.

Methods: Subjects performed a visual discrimination task, having to determine the orientation of a target array of three bars located at the lower-right quadrant of the visual field, such that the target falls onto the peripheral part of the retina outside the fovea (Figure 1). The task was performed in three consecutive days. During the second day subjects received cortical V1 or control vertex stimulation using the rTMS immediately following a short reactivation session of the task. The cluster of V1 was determined using a localizer fMRI scan. Stimulation was delivered using a frameless stereotactic neuro-navigation system. We hypothesized that learning following V1 stimulation would be impaired in comparison to a normal learning curve following control stimulation.

Results and conclusions: The fMRI localizer resulted in a reliable cluster of activation within the anatomical boundaries of V1. Regarding stimulation, subjects in which V1 was stimulated showed variable learning effects, with more subjects needed to complete the study and test our hypothesis.

Keywords: Perceptual Learning, rTMS, Visual-fMRI.

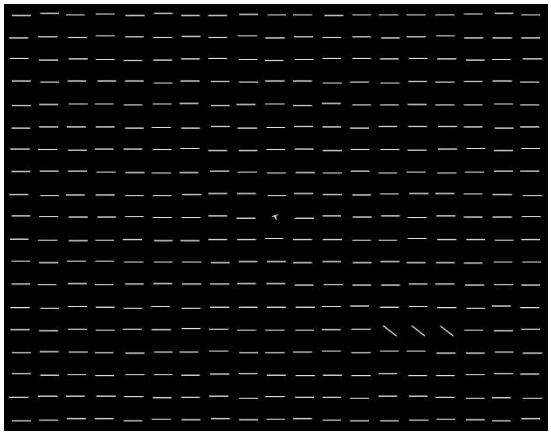

Figure1 : Target screen as displayed during the experiment

(6)

Acoustic Characteristics of the Thoracic Diaphragm for Focused Ultrasound Treatment of the Liver

Roana Schiopu[1], Limor Arbel[1], Hanan Khamis[1], Lilach Shay[2]

[1]Department of Biomedical Engineering, Technion - IIT, Haifa, Israel
[2]InSightec Ltd, Tirat Carmel, Israel

Introduction: According to 2015 American Cancer Society statistics, liver cancer is in the top 10 most common cancers and top 5 most common causes of cancer death. ExAblate² system is using Magnetic Resonance guided Focused Ultrasound (MRgFUS), a revolutionary non-invasive therapy method of tissue ablation. As part of continuous research, InSightec has developed interest in liver tumor therapy. In 2010, the company performed a pre-clinical trial on a healthy grown porcine which included high energy level sonications focused on the liver. Post-trial autopsy showed internal rib burns with no confirmed cause [Figure 1a]. A leading hypothesis was that the diaphragm, which is located between the liver and the ribs, interferes with the propagation of the ultrasound beam through it, causing undesired over-heating of surrounding tissues. Our aims in this study were (1) to estimate the acoustic attenuation of the thoracic diaphragm in order to either strengthen or refute the previous hypothesis (2) to predict temperature rise along the diaphragm as a function of therapeutic parameters for liver treatment benefits.

Methods: We performed two different ex-vivo post-mortem experiments on three porcine diaphragms; the first was executed using the ExAblate² system including MR (1.5 T) compatible FUS transducer (1.15 MHz), and soft tissue simulating phantom which was located on top of the diaphragm. Multiple 20 seconds continuous sonications were performed through degassed water using different acoustic powers at multiple locations on the phantom. The second experiment was conducted using 1.15 MHz hydrophones system in order to record transferred ultrasound wave signals through the ex-vivo diaphragm. The signal analysis was performed using LabVIEW and MATLAB software.

Results: In the hydrophones experiment, we analyzed the received pressure phasor of the ultrasound wave and calculated the signal amplitude as a function of transmitted frequency. We then evaluated the attenuation percentage caused by the diaphragm in relative to water reference; the average value for the tested diaphragms was 2.53±0.75% [Figure 1b].

For the ExAblate² experiment, our findings showed that a temperature of 50°C, which is considered as tissue ablation threshold temperature for 20 seconds sonication, was obtained when energy density on the diaphragm got to 144 [J/cm^2]. This energy density can be reached, for example,

when 2000J sonication is transmitted to a target located at 20 mm distance from the diaphragm [Figure 1c].

Conclusions: Results showed minor attenuation caused by the diaphragm relative to water, refuting the hypothesis that the diaphragm interferes with the propagation of ultrasound waves through it. According to our experiment data analysis, liver tumor therapy can be safely conducted for a minimal distance of 2 cm from the diaphragm, while for closer tumors there is a need to take into account energy density level considerations [Figure 1d]. Nonetheless, this study was conducted on ex-vivo tissue which lacks important in-vivo parameters such as blood perfusion and metabolic processes, and was exposed to inevitable system errors such as air bubbles and thermometry noises. This work will assist InSightec[2] to go forward with liver tumor therapy research and development.

Keywords: Thoracic diaphragm, high intensity focused ultrasound, acoustic attenuation, ablation

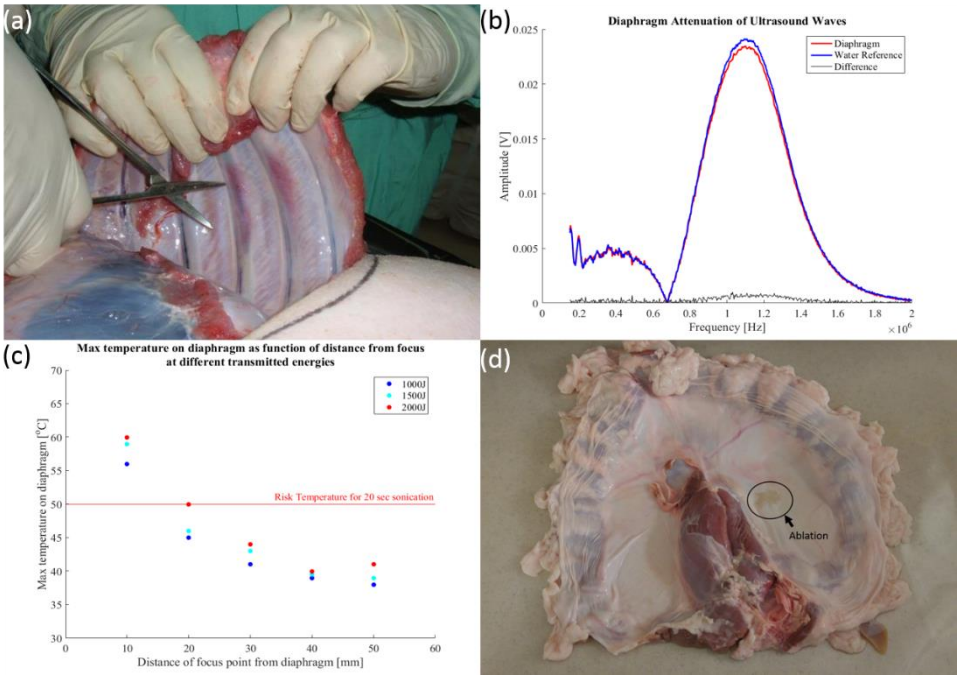

Figure 1: Thoracic diaphragm analysis for liver tumor therapy. (a) Post trial autopsy on a grown porcine following in-vivo focused ultrasound experiment on the liver showed internal rib burns. (b) Hydrophones experiment plotting of transferred ultrasound wave amplitude as a function of transmitted frequency, both through the diaphragm and water reference. (c) ExAblate experiment data analysis describes the maximal temperature detected along the diaphragm as a function of target distance from it, for three therapeutic energies applied. (d) Post trial ablation detection on the diaphragm caused by high level energy density sonications.

(7)

Early Assessment of Heart Function from Mitral Annulus Plane Excursion (MAPE) Semi-automatic Tracking

Hadas Avraham[1], Uri Goldsztejn[1], Grigoriy Zurakhov[1], Hanan Khamis[1], Zvi Friedman[1 2]

[1]Department of Biomedical Engineering, Technion - IIT, Haifa, Israel
[2]General Electric: Healthcare, Tirat Hacarmel, Israel

Introduction: Reduced long-axis deformation, e.g. as derived from the temporal excursion of the mitral annulus plane correlates well with left ventricle systolic and diastolic dysfunction. Since this parameter is only slightly compensated at the offset of cardiac disease, it is proposed as an early marker of cardiac disease. The lack of an instant, yet accurate tool for MAPE evaluation prevents this measurement from being used routinely in the clinic. An algorithm was developed for semi-automatic tracking of the mitral annulus and implemented in a MATLAB code. It was applied on apical two chambers echocardiograms. An auxiliary tool for temporal mitral valve opening and closing has also been developed, implemented and used for parameter optimization.

Methods: The proposed algorithm is based on block-matching in the complex gradient domain. The input video's frames are processed with a non-local means and median filters, and then undergo gradient extraction. Each pixel is assigned a phasor, composed of the magnitude and direction of its gradient. Afterwards, the user is required to mark the initial positions of the apex, the mitral valve and basal point (Figure 1). The position of the basal point is iteratively searched for, in the consecutive frames. The search is related to the physiological phase in the heart cycle. The present physiological phase is determined from the position of mitral valve. For improved results, the search is also done starting at the end of the video. Different initial points, in close proximity to the selected one, are tracked and the best result is chosen. This is crucial for the cases of human operator's slight inaccuracy in the selection of initial position.

Results: During the development phase, the algorithm's parameters were optimized so that the results matched the manually marked paths. To evaluate the algorithm's performance a data set (n=25) including twenty new videos was used. The curves obtained were also compared with the global strain obtained with the commercial program Echopac, developed by GE Healthcare. The results were evaluated according to the cross correlation obtained, since both algorithms measure different patterns that behave very similarly. The average correlation obtained was 0.92, with a standard deviation of 0.038.

Conclusions: The obtained results support the implementation of the developed algorithm in commercial ultrasound equipment. The graphs obtained correlate well with strain curves. Since algorithms used to obtain strain curves are usually computationally heavier the presented algorithm

is suggested as an alternative. An adaptation of the presented algorithm for right ventricle function evaluation can lead to a novel test for pulmonary emboli.

Keywords: Heart Failure, Strain curves, Semi-automatic Tracking.

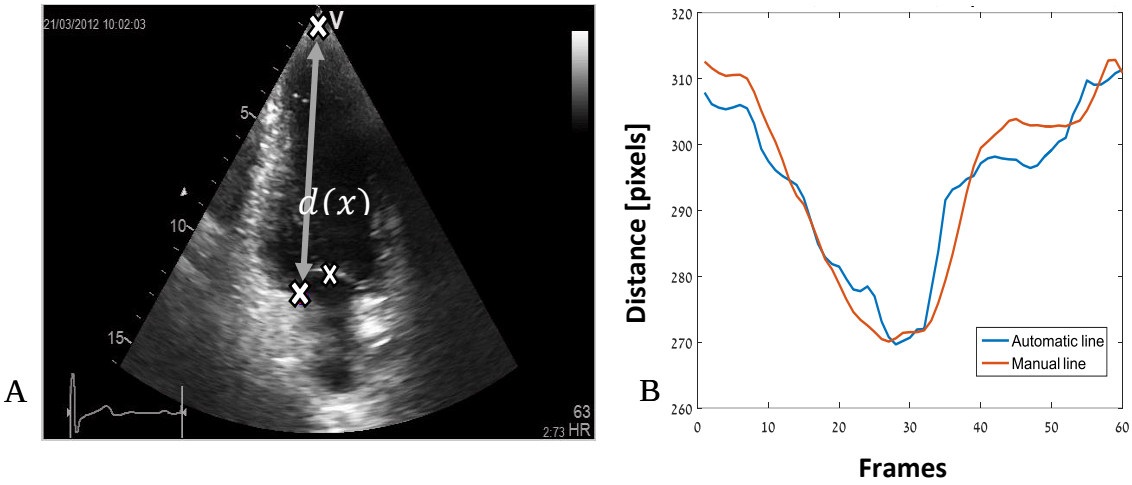

Figure 1: A. The basal point (at the center of the image) is tracked throughout the video and the distance from it to the apex is calculated. The mitral valve point position is indicated. B. The obtained line (in blue) is plotted with a manual marking of the basal point position in each frame (in red). The cross correlation between the curves is 0.96.

(8)

Sensory Feedback – Raptor Reloaded

Yair Herbst[1], Moran Davoodi[1], Oscar Lichtenstein[1], Yoav Medan[1,2]

[1] Department of Biomedical Engineering, Technion - IIT, Haifa, Israel
[2] Haifa3D Organization, Haifa, Israel

Introduction: The raptor reloaded is a basic hand prosthesis designed mainly for children with an amputation above the wrist. The mechanism converts wrist movement into flexion and extension of the fingers. The design is offered for free and manufacturing of the hand is very cheap (~$40). This makes the Raptor hand a great solution for many and especially for children who are constantly growing out of their prosthesis. The main drawback of the Raptor Reloaded and prosthesis in general is the lack of sensation e.g. textures, temperature etc. In addition the design doesn't fit any anatomical abnormality and lacks the ability to grasp small objects. Researchers suggest that the addition of sensory feedback could have a significant psychological effect since most of potential recipients were born without a fully functioning hand and would now be able to feel.

Methods: In order to add the missing sensory component, while minimizing the effects on the current benefits of the design, we offer a solution comprised of four components: 1. Sensing- pressure, location and temperature sensors which are all based on variable resistance response. 2. Logging and analyzing- Arduino Nano interface based on ATmega328 chip. 3. An electronic, multi-sensory feedback system- comprised of two servo motors, a vibration motor and an RGB led. 4. A mechanical feedback system- consists of 4 rods and provides texture sensing. An emulator was also developed in order to check the design in various stages. In addition, a number of modifications were done to the current mechanical design in order to improve it, including a new thumb design, reduction of friction and a themo-forming brace for a personalized hand.

Results: The final design serves its purpose and main requirements are met. It is based on standard off-the-shelf parts which maintains the high availability and low cost of the original design, as most of the parts can be reused when the recipient grows out of his hand. Additional cost is ~$50 for the first hand and another ~$10 for every new one. The circuit can run a full day without recharging and the weight of the entire hand increased by ~150gr. On the other hand, the assembly process is time consuming (~15hr) and requires technical background. Preliminary results show an ability to sense gripping strength and textures using our modified model.

Conclusions: We developed a sensory feedback system, and improved the mechanical model. The entire process needs to be integrated through the recipient's brain so additional testing is required after a sufficient adaptation time. Future research regarding the learning curve and adaptation

could provide interesting insights and an extensive design work is required in order to further improve the mechanical model. Future designs should incorporate the sensory system with a motorized hand.

Keywords: Low cost prosthetic, Haptic feedback, Brain machine interface, 3D Printing.

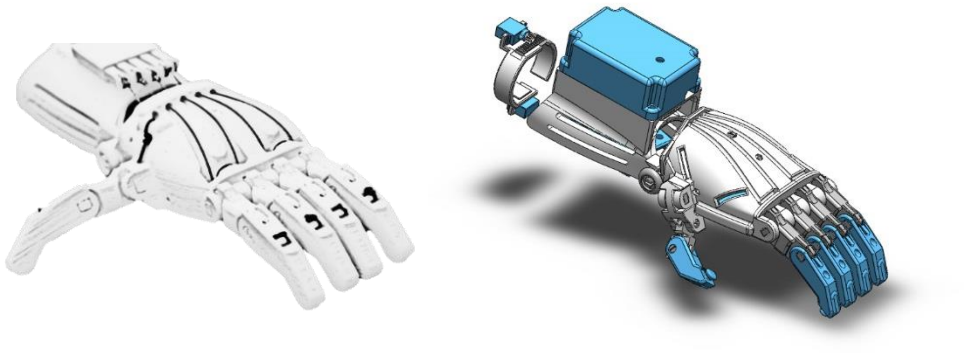

Figure 2- The original design (Left) and The Sensory Feedback Raptor Reloaded (hand and feedback band) (right). Improvements include: Sensory system, leaver, friction, pesonalized fitting and an opposable thumb.

(9)

Characterization of Mechanical Properties of the Hydrogels under the Different Values of Applied Physiological Stress

Ekaterina Gurevich[1], Yael Diamant[1], Yulia Merkher[1], Oscar Lichtenstein[1], Daphne Weihs[1]

[1]Department of Biomedical Engineering, Technion - IIT, Haifa, Israel

Introduction: Living tissues exhibit a broad range of stiffness, from less than 1kPa in brain for up to 10GPa in bone. Recently characterization of the mechanics of extracellular matrix and cell – matrix interactions have become the main subject of interest. However it is hard to obtain relevant data about specific parameter from tissue sample. Polymer materials offer advantages over natural materials, such as better control over material properties including mechanics, degradation rate and porosity in cell experiments. Several synthetic materials are commonly used in such experiments, including polyethylene glycol (PEG), polyacrylates, silicon and polyfumarate based gels. Measurements of mechanical properties of the hydrogels could be established by rheology, indentation technic, supersonic shear imaging (SSI), compression test and etc. The aim of this study was to further delineate mechanical properties of hydrogels with different stiffness values. We used synthetic polyacrylamide gel in order to segregate the mechanical factor and to eliminate the influence of the extracellular matrix composition. Subsequently in our study mechanical testing modalities are systematically compared for the same gels, in order to establish best practices for both experimental protocol and data analysis methodology.

Methods: In all our experiments we used synthetic impermeable polyacrylamide hydrogel. We prepared the gels with a stiffness range of 1.25 - 4.3 kPa that mimics physiologically relevant tissue elastic modulus. We preformed number of experiments using rheometer for time sweep and strain sweep tests and Instron for uniaxial tensile tests. In order to optimize the tensile test in the Instron we used SolidWorks to design two compartment dumbbell shape molds and appropriate grips. All parts were late printed using 3D printer using ABS – PC filament and PLA filaments.

Results: From the time sweep experiment we obtained the polymerization time. We used strain sweep in order to establish the extent of the material linearity - to find the viscoelastic region of the polyacrylamide gel. The uniaxial tensile test was used to obtain characteristic stress-strain curve and to find the yield and ultimate stress.

Conclusions: There is a high significance in choosing appropriate gel with well-known and highly predictable mechanical properties to specific experiment in order to exclude its influence on the net test results. We have not sufficient data yet in order to make a conclusion about the mechanical properties of polyacrylamide hydrogel.

Keywords: Polyacrylamide hydrogel, mechanical properties, instron, rheometer.

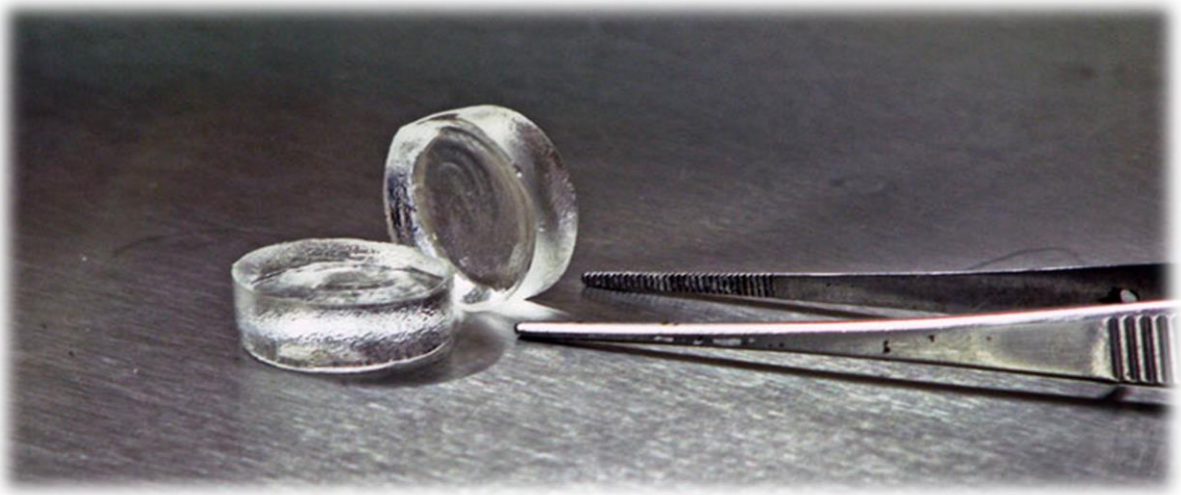

Figure 1: Hydrogel sample.

(10)

Development of Applicative Methods for Reliable Portable and Real Time Control of 3D Printed Hand Prosthesis Using Surface EMG Signals

Aviv Peleg[1], Or Dicker[2], Oscar Lichtenstein[1], Tal Shnitzer[2]

[1]Faculty of Biomedical Engineering, Technion - IIT, Haifa, Israel
[2]Faculty of Electrical Engineering, Technion - IIT, Haifa, Israel

Introduction: Hand prosthesis with embedded control and multiple gesture type can reach high prices, and offer less flexibility and patient specific adjustments. With the introduction of 3D printing, many open source designs for prosthesis emerged, most of them with a single type of hand movement and limited control of the hand. In this research we aim to develop an accessible 3D printed hand with a control mechanism which is reliable, portable, real-time and controllable.

Methods: The prosthesis used was an upgraded version of an open source hand from e-enable, modified to be powered from 3 servo engines, and not from the movement of the Hand Stump. The offline classification algorithm was developed using Matlab, MathWork Inc., it was designed to fit both real time requirements (less than 250ms) and high reliability while using low frequency sampling rate. Different features(moving absolute Value ,Root mean square, Willison amplitude, Modified Mean Frequency, wavelet coefficients) and Different machine learning methods were tested (support vector machine with different kernels, k-Nearest Neighbor with different k) to reach maximum accuracy. Different recording methods (stationary hand gestures, moving hand gestures), were tested to make the learning process short and efficient .Real time implementation of the algorithm was performed on Intel Edison using Python. We utilized the MYO Armband sensors that were connected via Bluetooth to the Edison system. The MYO Armband has a sampling frequency of 200Hz, which is significantly less than then the golden standard of 1-2kHz.

Results: The proposed algorithm yielded a classification rate of 99% using recordings of stationary hand gestures, while the recording of moving hand gestures achieved success rate of 96%. Several feature extraction methods in the time domain achieved the same successful results, while most of the feature extraction methods of frequency domain were unsuccessful most likely because of the low sampling rate. The method chosen as the best was Moving Absolute Value. The machine learning method with the best results for this given data is the k-Nearest Neighbor, with k=3.

Conclusions: The proposed method achieved high accuracy of prosthesis movement classification. The only challenge left in this method is the high price of the currently used shelf product. Several techniques for price reduction were examined and should be validated in the near future.

Keywords: EMG, Prosthesis Control, Machine Learning.

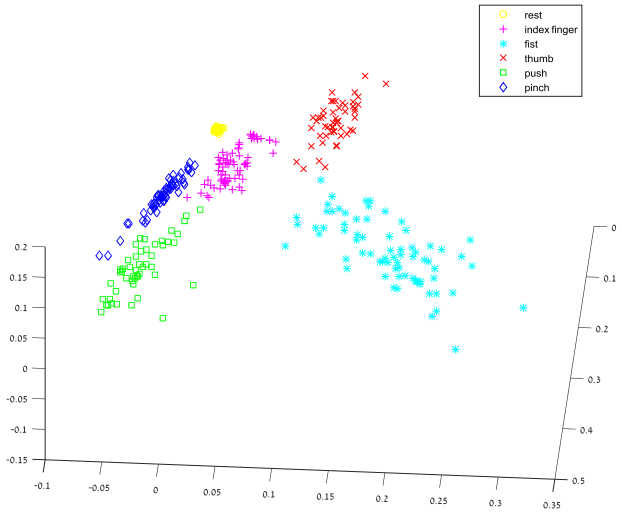

Figure 1: ***Data after feature extraction and PCA, showing the 3 main dimensions***

(11)

Enzyme-Based Bioreactors: Therapeutic and Industrial Applications

Tamara Shor[1], Adina Shatz[1], Yathreb Assad[1], Daphne Weihs[1], Noah Lotan[1]

[1]Department of Biomedical Engineering, Technion - IIT, Haifa, Israel

Introduction: Enzymatic bioreactors have wide applications in industries, including pharmaceuticals, food and agriculture, as well as in medicine. The enzyme β-Glucosidase is of particular interest since β-Glucosidase is lacking in patients with Gaucher's disease, a genetic disorder that affects organs throughout the body. Also, this enzyme has various industrial applications, such as in food, biofuel and agriculture.

The aims of our research activities were: (a) To design, assemble and operate immobilized enzyme-based bioreactor systems, using β-Glucosidase as a model enzyme; (b) To determine the performances of these systems for a variety of operational parameters; (c) To interpret the results obtained in terms of engineering models of their functional characteristics.

Methods: For enzyme immobilization, we used the Duolite A658 resin and silica particles as insoluble carriers. Glutaraldehyde was used as a coupling reagent. The self-controlled Soxhlet system and active charcoal treatment were used for purification of the Duolite A658 resin and of glutaraldehyde, respectively.

The reactor itself was built as a packed bed unit, and operated in the continuous mode. The substrate employed was p-Nitrophenyl-β-D-glucopyranoside, while a colorimetric assay using spectrophotometer was used to quantitate the enzymatic activity.

The results obtained were interpreted in terms of appropriate engineering models and used to determine the operational characteristics of the system at hand.

Results: We designed and built multiple enzyme-based bioreactors. They involve: (a) A metering pump, which we previously calibrated; (b) The bioreactor itself, disposable syringe containing a packed bed of immobilized β-Glucosidase; (c) A programmable fraction collector. The systems

were operated in the continuous mode. The product concentrations in the outlet fractions were measured by spectrophotometer and used to determine the conversion rate and productivity achieved for different operational parameter values.

We found that the functional characteristics of the systems, inter alia, depend on the substrate concentration, flow rate of the inlet feed, as well as on the dimensions of the bioreactor. Moreover, the optimal bioreactor studied was found to be relatively stable, retaining about 60% of the initial activity rate after 5 months.

Conclusions: Immobilized enzyme-based bioreactor systems can be designed and assembled in various configurations. When operated in the continuous mode, the system performance depends on the operational parameters applied. Hence, such systems can be engineered according to the particular application considered, be it in the medical or industrial field.

Keywords: Bioreactor, Immobilization, Enzymatic Activity

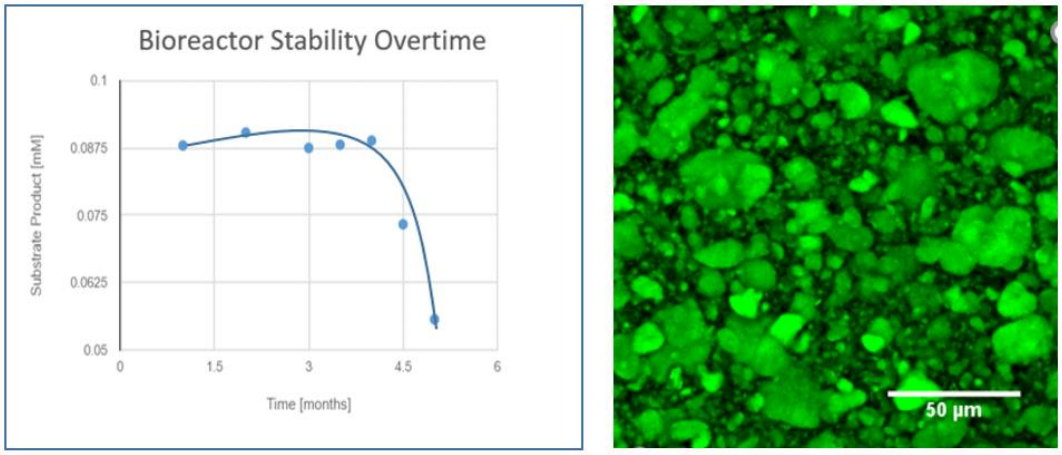

Figure 3: Graphical representation of the stability of the bioreactor (left). Representative example of an insoluble carrier with a silica albumin attachment (right).

(12)

A 3D Cell Expansion System of Pericytes Using Fibrinogen Based Hydrogels for Muscle Tissue Regeneration

Avi Izraeli[1], Yair Hochner[1], Nasma Mazzawi[1], Olga Kossover[1], Dror Selektar[1]

[1]Department of Biomedical Engineering, Technion - IIT, Haifa, Israel

Introduction: Degenerative muscle diseases which cause muscle loss can be treated with therapeutic treatments, e.g. physiotherapy, or by cell injection. Skeletal muscle tissue engineering is a promising approach for the treatment of muscular disorders. Pericytes are perivascular cells that envelop capillary endothelial cells, and are known to differentiate toward myogenic lineage. Recent studies show that they have a profound impact in skeletal muscle regeneration.

Pericyte culture in petri dishes has been performed successfully (*in vitro*). Yet, culture methods still need further optimization, to meet the large scale demand for commercial clinical application. In order to outstand the culture methods, in this work, we attempted to determine the feasibility and optimal conditions of pericyte culture in hydrogel microcarrier 3D cultivation system. Polyethylene glycol-fibrinogen (PF) microcarriers are biocompatible and provide a precisely controlled environment. Additionally, the culture processes in PF microcarriers are much more simple and cost-efficient, since only one-time seeding process is needed, and all intermediates processes can be handled by a stirred suspension bioreactor.

Methods: Pericytes were cultured with conventional methods (in 10cm petri dishes) for 1 week to stimulate cell growth. Healthy pericytes were then added to PF hydrogel and formed as beads of ~2mm diameter. Samples were made with different G-modulus (gel stiffness), and different cell concentrations.

All samples were examined on days 1,3,7,10,15, and 22. Zeiss Lightsheet Z1 microscope was used to perform viability analysis, using Hoechst/PI staining. Images were analyzed using Imaris software. Additional samples were stained with Calcein/Ethidium and analyzed with Zeiss confocal microscope.

Results: Cells showed good signs of growth and proliferation in most samples, as can be seen in figure 1 below. Additional lightsheet viability analysis was performed.

Conclusions: PEG-Fibrinogen hydrogel appears to be a good medium for pericytes growth. Pericytes appear to proliferate in our 3D culture. However at low G-modulus, beads appear to fall apart, therefore future assay should focus on gels with G-modulus $\geq$500 [Pa] .

Optimal conditions for pericytes growth can be determined once further analysis is performed. Additional analysis, which involves immunostaining to insure our cells did not differentiate during our experiment, is currently under progress.

Future work should be done to test the possibility of growing pericytes in beads inside bioreactors in larger scale. Additional experiments must be performed to insure that these cells can be forced to differentiate into muscle cells, and that once differentiated, muscle tissues can be assembled and implanted back in patients.

Keywords: Tissue Engineering, Pericytes, Polyethylene glycol-fibrinogen

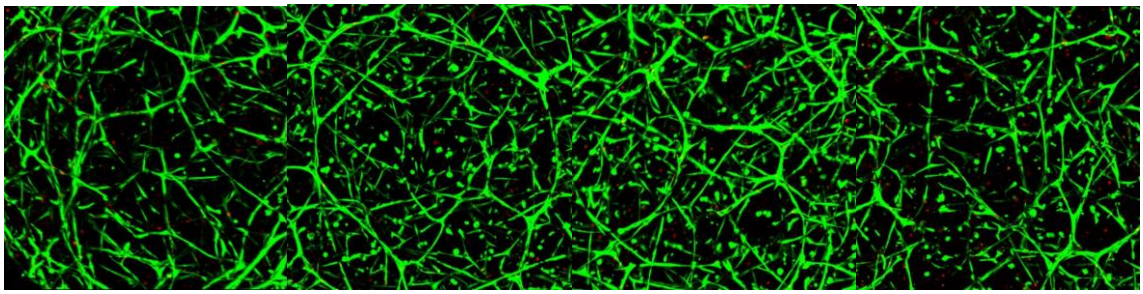

Figure 1: Calcein/Ethidium assay results of day 21. From left to right: 250, 500, 750 and 1000 [Pa] (G-modulus of gel). Images show good proliferation of cells (green) and low number of dead cells (red).

(13)

Implementation of 8 MeV Total Skin Electron Irradiation Based on the Stanford Technique

Reut Guy[1], Chen Avraham[1], Alex Vilensky[1], Shahar Daniel[2]

[1]Department of Biomedical Engineering, Technion - IIT, Haifa, Israel
[2]Department of Radiation Oncology, Rambam Health Care Campus, Haifa, Israel

Introduction: Total skin electron irradiation (TSEI) is one of the most effective treatments for Cutaneous T-cell lymphoma (CTCL). The treatments for CTCL in the oncology department at Rambam Health Care Campus use 6 MeV electron beams, and are based on the Stanford technique. In some cases, the therapeutic range achieved with such energy is insufficient for obtaining remission of the disease**.** Therefore, a higher energy beam should be applied in order to effectively treat thick skin lesions without increasing damage to normal tissues. The purpose of this study is to implement high dose-rate 8 MeV electron beam irradiation for TSEI based on the Stanford technique.

Materials and Methods: Electron beam irradiations were carried out using the Elekta Precise linear accelerator. Measurements were performed for energy calibration and percentage depth dose (PDD) curve characterization at source-surface distance of 100 cm (SSD=100cm), determination of the optimal dual angle, full treatment characterization, and absolute calibration. In addition, the dose and energy spectra of the X-ray contamination were characterized, and the efficiency of the shielding devices for the head, legs, palms and eyes was evaluated. Measurements were performed using a PTW computerized water phantom equipped with Semiflex (31010) ion chambers, a solid water phantom (RMI-457), an anthropomorphic phantom, Roos and Farmer ion chambers connected to a Farmer 2570 or PTW UNIDOS electrometer, EBT3 radiochromic films, and thermoluminescent dosimeters (TLD-100). An Epson expression 10000XL photo scanner and the ImageJ software were used to digitize and analyze the radiochromic films. TLDs were read using a Harshaw TLD^{TM} 3500 photomultiplier. Statistical analysis using the Student's two-tailed t-test was performed to validate the measurements.

Results: The optimal dual-field angle was found to be 17°. Vertical profile uniformity was within ±7% along a distance of 200 cm, and the horizontal profile uniformity at the level of isocenter was within ±5% along a distance of 60 cm. The depth of the 80% isodose (R80) for the full treatment was 1.55 cm. The twelve field factor was found to be 3.4. The X-ray contamination dose was 0.7% of the treatment prescription dose. Mean photon energy of the X-ray is ~1.5 MeV. Shielding

devices used for protection against the 6 MeV beam were found to be sufficient for the 8 MeV beam.

Conclusions: The 8 MeV electron beam therapy enables higher penetration than that achieved with the 6 MeV beam. The higher penetration depth allows treating advanced stages of CTCL while maintaining a uniform dose distribution and low X-ray contamination.

Keywords: Cutaneous T-Cell Lymphoma, Total Skin Electron Irradiation, Stanford Technique

Figure 1. Performing a dosimetric characterization of the total treatment using an anthropomorphic phantom.

שלום רב,

אנו שמחים להציג בפניכם את תקצירי הפרויקטים של הסטודנטים המסיימים לימודיהם בשנה זו, שנת תשע"ו.

הפרויקט, המבוצע ע"י סטודנטים בשנת הלימודים האחרונה, מהווה את גולת הכותרת של לימודיהם לתואר בהנדסה ביורפואית.

במסגרת הפרויקטים, מביאים הסטודנטים לידי ביטוי את הידע והכלים שרכשו במהלך השנים בתחומי ההנדסה, המדע והרפואה.

מטרת הפרויקטים, הינה לתת מענה לצרכי הפיתוח והמחקר של חברות העוסקות בתחום ההנדסה ביורפואית, תוך עמידה בסטנדרטים המקובלים ובמקביל, לתת ניסיון ואתגר מקצועי לסטודנטים המסיימים ולעודד השתלבותם בתעשייה הביורפואית.

לפרויקטים חלק חשוב בעידוד היזמות בקרב סטודנטים, וחלקם אף מובילים להקמת חברות הזנק ורישום פטנטים.

פרויקטים אלו מהווים נדבך מרכזי בחזון הפקולטה, לחתור לבניית גשר מצויינות ובמה לקשרים ושיתופי פעולה ארוכי טווח בין האקדמיה והחברות המובילות בתעשייה.

הפקולטה מאחלת הצלחה לסטודנטים המסיימים, ומקווה לראותם בעתיד נוטלים חלק פעיל בפרויקטים חשובים אלו כמנחים מהתעשיה.

בברכה,

פרופ' אמיר לנדסברג, דיקן הפקולטה

ד"ר אלכס וילנסקי, אחראי קורס פרויקטים

צוות הקורס: גב' חנאן ח'מיס, גב' ניסמה מזאוי וד"ר אוסקר ליכטנשטיין

הפקולטה להנדסה ביורפואית בטכניון

כנס פרויקטים
16 ביוני, 2016

תקצירים

הטכניון
מכון טכנולוגי לישראל