Antibacterial Nanofibrous Mesh- A Wound Healing Device for Complex Wound Treatment
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Introduction:
Despite the advances in medicine, healing of complex wounds remains one of the major health problems that affect billions of people each year worldwide. Many complication factors are the causes, including inflammation response, infection, and long-term healing period. Based on current understanding, the purpose of this study is to fabricate nanofibrous composite scaffolds consisting of nanoparticles loaded with various therapeutic reagents for wound healing applications.

Aims and Methods:
The aim of this project is to develop a nanofibrous mesh having antibacterial properties using Chitosan mixed with polyethylene oxide (PEO) and containing poly(lactic-co-glycolic acid) (PLGA) nanoparticles loaded with therapeutic reagents. The key elements are the formation of nanofibers as the bio-mimicry extracellular matrix (ECM) in human tissues, the inhibition of bacterial growth from Chitosan based materials, and the sustained release of therapeutic reagents including growth factors that are loaded or encapsulated in PLGA nanoparticles. The Chitosan-PEO meshes were characterized using scanning electron microscopy (SEM). Additionally, bacterial study was performed to determine the anti-microbial properties of these meshes. In vitro studies using human dermal fibroblasts were used to evaluate the biocompatibility of the nanofibrous composite meshes. Furthermore, in vivo studies using murine models were utilized to test the wound healing efficiency of the system.

Results and Conclusions:
The results revealed that the PLGA nanoparticles provided the sustained release of various growth factors including vascular endothelial growth factors (VEGF) and basic fibroblast growth factors (FGF), while the fast releasing Chitosan-PEO mesh provided a support that promotes angiogenesis. Additionally, in vitro studies demonstrated the success in promoting cell proliferation while providing antibacterial properties. More importantly, the in vivo studies showed accelerated wound healing process. Histology of animal wound tissues indicated that our composite system increased the amount of granulation tissue and thickness of epithelial layer more than the open wound control and the commercial product in short term. A higher percentage of collagen deposition was also observed in the wound area with our system. Thus, this nanofibrous mesh can be potentially used for the development of an effective complex wound healing system.
NANOCOMPOSITE TRANSDERMAL HYDROGEL SYSTEM FOR SKIN CANCER AND WOUND HEALING TREATMENT
Pranjali P. Tambe, Jyothi U. Menon, Dr. Kytai T. Nguyen

Introduction:
Melanoma skin cancer is the most dangerous form of skin cancer and the major cause of deaths related to skin cancer worldwide. Conventional treatment such as chemotherapy has several disadvantages, such as low response rate, low patient compliance, severe side effects and development of multidrug resistance. We developed a nanocomposite transdermal hydrogel system incorporating stimuli responsive nanoparticles with dual drug release capabilities and an anti-bacterial drug to prevent wound infections for skin cancer therapy.

Aims and methods:
The aim of the system was to develop a transdermal nanocomposite system with dual drug release to overcome multidrug resistance and provide the necessary requirements for an ideal wound healing bed. This hydrogel system consists of the polymer PEGMC (Polyethylene glycol maleate citrate), the crosslinker PEGDA (Polyethylene glycol diacrylate), initiator Ammonium persulphate, and accelerator Tetramethylethylenediamine. Factorial analysis was done on the hydrogels to check the effects of formation factors on the different properties of the hydrogel to select the optimal hydrogel for use in our composite system. In order to do this, hydrogels were optimized by taking three different molecular weights (3.3K, 6K, 8K) of PEGDA and varying concentrations of APS and TEMED. Drug release study was carried out over a period of 14 days using model drug Bovine Serum Albumin. Further, PLGA (Polylactic-co-glycolic acid) conjugated with CMC (carboxymethyl-chitosan) via EDC-NHS chemistry was used to form pH-responsive polymer PLGA-CMC nanoparticles, which were embedded inside the hydrogel.

Results and discussion:
Curing time for PEGMC-PEGDA (3.3K) was around 2-3 minutes. The swelling ratio study for the same combination confirmed that hydrogels had a swollen ratio of 99±0.32 which was measured by weighing the swollen weight and the dried weight of hydrogel. Drug release profile showed burst drug release for a period of 3 days from hydrogel. The future work includes optimizing hydrogel system, nanoparticle characterization as well as in-vitro and in vivo testing of this nanocomposite hydrogel.
Fibrocyte / collagen orientation to PDMS micropillar implants
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Introduction: Surface topography has been shown in many studies to alter cellular and tissue responses, although the mechanisms governing such reactions are not entirely understood. With the recent development of micropillar surfaces, the influence of surface roughness on cellular responses can now be systematically evaluated. The depth of and distance between pillars were found to have significant effects on implant-mediated tissue responses in vivo. Surprisingly, the micropillar-mediated tissue responses are governed by fibrocytes, but not macrophages. The initial interactions between fibrocytes and micropillar substrates may dictate and direct fibrotic tissue formation and structural organization.

Aims and Methods: PDMS micropillar films were generated in a hexagonal geometry with various height and spacing characteristics. These films were then tested in vitro, comparing macrophage and fibroblast cell line behaviors. Subsequently, films were implanted in vivo and the resultant tissue responses were analyzed. Birefringent collagen analysis reveals differences in fibril alignment. By controlling the spatial arrangements of micropillars, the tissue response is altered due to the cellular interactions of migrating pro-inflammatory fibrocyte cells.

Results and Conclusions: Micropillar arrays have a significant influence on fibroblast and MΦs both in vitro and in vivo. We found that the increase of pillar height (but not pillar spacing) enhance fibroblast proliferation while the decrease of pillar spacing (but not pillar height) reduce MΦ accumulation in vitro. In spite of these extreme cellular responses, all pillar substrates prompt distinct tissue responses in vivo. Of which, the collagen fiber alignment may be altered by the pillar orientation. This may lead to "optimal" arrangements specific for the designed application, such as anisotropic tissues.

Figure 1: micropillar films are responsive to fibrocytes correlating with collagen production. Birefringence reveals alterations in fibril alignment at the interface with pillars.
A dielectrophoretic method for separating cancer cells from tumor cell populations

Victoria Holderby and Shalini Prasad

Cancer stem cells are the main source of new cancer cells within a tumor which also resist treatment, so there is an urgent need for characterization of these cells to create new treatment methods. Characterization requires separation from cancer cell populations in a tumor mass.

The long term goal of this project is designing a new approach for separating rare cancer stem cells in a fast and non-invasive manner using a microelectrode based device. The technique used is dielectrophoresis (DEP), which moves cells using a non-uniform electric field based on dielectric properties specific to the cell and suspending medium. Cell separation using fine resolution DEP is accomplished by applying a voltage and specific frequency to an electrode pattern creating an electric field inducing a DEP force influencing the movement of the targeted cell. The electrode design was a simple 2x2 array with alternating positive and negative terminals having a diameter of 250 microns and center to center distance of 750 microns, creating high electric flux at the electrode edges for the target cells to gather. While the target cells are held in positive DEP at electrode edges, the unwanted cells are forced to the middle of the array by negative DEP, effectively separating the cells.

The electrode pattern was optimized through 3D COMSOL modeling, while the particle medium interaction was optimized through MATLAB computational modeling. The proof of feasibility for this device was done with polystyrene beads initially and then with HEK and HeLa cells. Unlike other DEP based technologies which lack sufficient resolution to achieve cancer cell separation in complex samples efficiently, this technique leverages the fine spatial resolution of the electrode design to achieve cancer cell separation. This configuration establishes a platform for optimization to separate cancer stem cells. With this technology, cancer diagnosis can advance more efficiently.
Breast cancer classification using impedance biosensors
Anjan Panneer Selvam and Shalini Prasad

Introduction:
Breast cancer affects one in eight American women over the course of their lifetime and is second only to lung cancer in the number of female cancer deaths per year. It is not considered a life-threatening disease until after it has spread systematically. Survival rates range from 88% to 15% depending on stage of the cancer. Cancer stem cells provide significant information for understanding prognosis, which can help develop better treatment strategies.

Aim and Methods:
We adopt the cancer stem cell (CSC) hypothesis that classifies tumor populations into: invasive cells (high CSC activity) and non-invasive cells (low CSC activity). The aim of the study is to quantify protein concentrations in CSC lysates against three specific markers: (a) Platelet derived growth factor (PDGF-R), isozymes of aldehyde dehydrogenase (b) ALDH1A1 and (c) ALDH1A3. Current immunoassay and western blot techniques are not sufficiently sensitive as well as selective for the application of cancer risk classification based on protein quantification of CSC’s.
This project describes the design and validation of a sensor which is an electrical immunoassay that mimics the principle of “macromolecular crowding” to achieve size based nano confinement of proteomic markers. Electrochemical Impedance spectroscopy has been employed and impedance changes due to protein binding events at the electrode–solution interface are used to quantify protein concentration levels in CSC lysates.

Results:
This sensor demonstrates classification of the two tumor cell populations based on proteomic activity to the three biomarkers. Test lysate samples from SUM159, HCC1143 and DCIS cell lines were quantified based on levels of protein markers. Low concentration (ng/mL regime) detection is demonstrated in a label-free process. It is observed that ALDH1A1 at a concentration of 250 ng/mL provides best classification of the protein markers. This technique can prove to be a significant resource for rapid diagnosis of protein biomarkers at clinically relevant concentrations.
A Novel Nanotexturing Approach for Early Detection of Cardiac Risk

Michael T. Jacobs and Dr. Shalini Prasad

One hundred thousand patients undergo surgery daily in the United States, 33 million annually, at a cost of $450 billion. Troponin-T is a biomarker that has been associated with increased mortality following vascular surgery. The project goal is to design a technology for Troponin-T, enabling identification of high risk surgical patients as candidates for intensive medical management and surveillance. Currently there are a number of label-free technologies for Troponin-T detection, however they possess limitations including insufficient sensitivity and a lack of robustness. These drawbacks are primarily attributed to the substrate and nano materials used in construction and assay development process.

The technology being detailed demonstrates the feasibility in integrating heterogeneous nanostructures based on the use of gold nanoparticles. This method requires the application of gold nanoparticles onto a gold concentric circular patterned glass substrate. The gold pattern, with working and counter electrodes, was fabricated using photolithography and sputter deposition. In both cases, a chrome adhesive layer is used to enhance binding of the gold to the substrate. This helps in providing basic electrical conductivity for signal input and output. The gold nanoparticles were conjugated with dithiobis succinimidyl propionate (DSP) for the purpose of enhancing the binding of proteins, which in turn helps improve sensitivity of biomarker detection. The DSP-linked gold nanoparticles are stamped onto the electrodes using a matching pattern stamp constructed from polydimethoxy silane (PDMS). As a control to validate efficiency of the nanotextured surface, a printed circuit electrode board is also used.

Impedance spectroscopy was used as the measurement strategy to identify specific concentrations of proteins. We demonstrate detection of Troponin-T antigen at the attogram per milliliter level as well as higher concentration scales. The use of gold nanoparticles shows significant enhancement in detection and also proves to be a robust methodology for application to label-free biosensors.
Thin-Layer Matrix Sublimation with Vapor-Sorption Induced Co-Crystallization for Sensitive and Reproducible SAMDI-TOF MS Analysis of Protein Biosensors

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Introduction
Immunoassays are widely used in biochemical/clinical laboratories owing to their simplicity, speed, and sensitivity. Coupling immunoassays on self-assembled monolayers (SAMs) to matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectrometry (MS) provides improved assay selectivity compared with traditional photometric detection techniques. We show that thin-layer-transfer (TLT) of α-cyano-4-hydroxycinnaminic acid (CHCA) MALDI matrix via vacuum sublimation followed by organic solvent-based vapor-sorption induced co-crystallization (VIC) results in unique matrix/analyte co-crystallization tendencies that optimizes assay reproducibility and sensitivity. Calibration curves for intact proteins are also possible over a broad concentration range and improved specificity of MS-immunoassays are highlighted by simultaneous label-free quantitation of ligand-bound protein complexes.

Methods
SAM immunoassays were prepared using gold-coated glass slides treated with NTA-terminated alkanethiolate, and incubated in Ni²⁺, Protein G, antibody, and biofluid containing antigen. For high-throughput arrays, gold slides were treated with parylene to form hydrophilic wells. The biochips were coated with MALDI matrix in a custom thin layer transfer (TLT) device at a pressure of ~120 torr over a period of 7 minutes. The dried polycrystalline matrix powder was then recrystallized in a custom vapor-sorption induced co-crystallization (VIC) chamber by exposure to methanol-saturated air. The TLT and VIC devices support up to 384 sample spots at a time for high-throughput, parallel processing. Samples were analyzed by Voyager DE Pro and ABI 4800 MALDI-TOF systems.

Results
We observed that CHCA microcrystals generated by methanol VIC resulted in >10× better sensitivity, increased analyte charging, and improved precision compared with dried droplet measurements. The uniformity of matrix/analyte co-crystallization across planar immunoassays directed at intact proteins yielded low spectral variation for single shot replicates (18.5 % relative standard deviation, RSD) and signal averaged spectra (<10 % RSD). We envision that TLT and VIC for MALDI-TOF will enable high-throughput, reproducible array-based immunoassays for protein molecular diagnostic assays in diverse biochemical and clinical applications.
Quantitative Measures Derived from Photoplethysmography for Enhanced Detection of Obstructive Sleep Apnea

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Introduction: Obstructive Sleep Apnea (OSA), a major sleep disorder which affects approximately 18 million US adult population can lead to dangerously low blood oxygen levels (hypoxia) due to absence of breathing. Hypoxia can create irreversible damage to the tissues and organs. Numerous studies have observed the oxygen saturation changes during apnea episodes using pulse oximeter, but few have studied the photoplethysmography (PPG) waveform. PPG reflects the blood volume changes in the micro vascular bed of tissue during apnea episodes.

Aims and Methods: In this study we aim to investigate the feasibility and efficacy of using the percentage oxygen saturation as well as the new features from the PPG waveform to detect and quantify the physiological changes due to apnea. Five OSA subjects (Age: 53.60±7.40 years, BMI: 33.66±7.27 kg/m2) were recruited for 8 hour nocturnal polysomnography study. For the continuous measurement of arterial oxygen saturation and PPG waveform, a forehead sensor based on reflectance spectrophotometry was used (Nellcor Oximax pulse oximeter, Nellcor Inc., CA). The features extracted are rate of drop of oxygen saturation, peak and valley of the waveform, area under the curve, amplitude and peak to peak time of PPG waveform.

Results and Conclusion: The mean drop of oxygen saturation was found to be -0.15±0.2 % (normal breathing), -26.69±4.4 % (apnea) and -11.25±1.5 % (hypopnea). Further amplitude of PPG waveform was 29.08±10.59 A.U (normal), 26.96±11.07 A.U. (apnea) and 26.13±10.60 A.U. (hypopnea). All the metrics except peak to peak time and area under the curve showed statistically significant difference between apnea and normal breathing (α=0.05). The results indicated that besides percentage drop in oxygen saturation, newly derived features from PPG waveform such as peak, valley, and amplitude may be useful for detecting the apnea episodes thereby enhancing the use of oximeter for screening subjects suspected of having sleep apnea, before incurring the cost of testing them in a sleep laboratory.
Correlations derived from Cerebral Blood Flow and Percentage Oxygen Saturation during Simulated Sleep Apnea

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Introduction: Obstructive Sleep Apnea (OSA) is the most common type of Sleep Apnea and is characterized by recurrent episodes of partial or complete collapse of the muscles in the Upper airway during sleep. The episodes are associated with a regular decrease in percentage oxygen saturations. The goal of this study is to investigate the variations seen in percentage oxygen saturation and cerebral blood flow during simulated sleep apnea, derive new features that are significant and can enhance the detection and quantification of physiological changes due to sleep apnea and also compare the different postures and protocols and derive significant features.

Materials and Methods: This study employed pulse oximetry, and Transcranial Doppler ultrasound to see the changes in cerebral blood flow and percentage oxygen saturation during simulated sleep apnea A group of 16 volunteers were recruited for the study (Age: 29.00 ± 4.86 years, Height: 165.88 ± 9.28 cm, Weight: 67.19 ± 19.31 kg and BMI: 24.07 ± 4.84 kg/m2). All the subjects were normal healthy subjects with no history of sleep apnea. They underwent the study for an approximate of 2 hours for 4 different protocols (Sitting 30s, 90s and Supine 30s, 90s). The features extracted from the oxygen saturation and cerebral blood flow waveform were: the peak and valleys of the waveform slope of the curve, area under the curve and the drop, rise and settling times during breath hold.

Results and Conclusions: The mean values obtained for Area are: Supine A 3.06±4.34 (A.U.) and Supine B: 2.38±2.25 (A.U.), Peak: Supine A: 0.864±0.082 (%SaO2) and Supine B: 0.874±0.068 (%SaO2) and Slope Supine A: 0.003±0.001 and Supine B: 0.003±0.001.The result using the Two-Way ANOVA and the Tukey Kramer pairwise comparison indicates, the above mentioned parameters are significantly sensitive to the duration of breath hold and other apnea effects.
Automated Sleep Pattern Monitoring for Sleep Disorder Assessment

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Abstract

Problem: Monitoring of sleep patterns is of major importance for various reasons such as the detection and treatment of sleep disorders, the assessment of the effect of different medical conditions or medications on the sleep quality and the assessment of the mortality risk associated with sleeping patterns in adults and children. Sleep monitoring by nature is a difficult problem due to both privacy and technical considerations. Current methods for sleep pattern assessment require the patient to spend one or more nights at a clinic which induces high costs and inconvenience for the patient. A method for sleep monitoring which is non-invasive, cost effective and can be used at home is highly desirable.

Methods: The proposed system uses a combination of non-invasive sensors to assess and report sleep patterns: a contact-based pressure mattress and a non-contact 3D image acquisition device, which can complement each other. To evaluate our system we used real data collected in Heracleia Lab’s assistive living apartment. Our system uses Machine Learning techniques to automatically analyze the collected data and recognize sleep patterns. It is non-invasive, as it does not disrupt the user’s usual sleep behavior and it can be used both at the clinic and at home with minimal cost.

Results: In our experiments we attempted to recognize body posture, while a user is sleeping, detect motion when it occurs and recognize the type of the motion by dividing it into a set of motion classes. Our experimental findings on real user datasets show that the task of analyzing sleep patterns with the intent to detect symptoms related to sleep disorders can be successfully achieved. Our classification methods achieved an average of 86.21% accuracy in recognizing the correct sleep body posture among 5 different classes (1. Back, 2. Left side, 3. Right side, 4. Stomach, 5. Sitting on bed), and an average of 89.07% accuracy in recognizing the type of motion among 4 classes (1. Changing body posture, 2. Moving arms or legs, 3. Getting in bed or out of bed, 4. Making bed).
Cytological Quantification of Metastatic Tumor Cells on Functionalized Chips

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Introduction: Cancer turns fatal when metastasis occurs from the spread of the rogue cells through blood stream. These cells, known as circulatory tumor cells (CTCs), eventually land on distant organs and form new tumors. Detection and enumeration of these CTCs in peripheral blood can be early cancer diagnosis modality. Given the commonality of enhanced EGFR expression in most cancerous cells, chips functionalized with anti-EGFR aptamer, to isolate the tumor cells can be used as a simple clinical laboratory testing device. The potential use of the aptamer-chip device for early cancer detection can save many lives.

Aims and Methods: Piranha cleaned glass slide surfaces were functionalized with anti-EGFR as well as mutant aptamer. Brain tumor cells, known as human glioblastoma (hGBM) and healthy glial cells, astrocytes, were transferred onto the surface and images were taken at every 20 seconds for 15 minutes. Quantitative analysis of cell behavior on EGFR-specific surfaces as well as control substrate was then performed using image analysis software. In short, after initial image enhancement, cell contour were detected and images were converted to binary for later processing. Temporal changes in cell contour were observed over frames and multiple feature vectors were calculated using binary converted images.

Results and Conclusion: Surfaces coated with anti-EGFR aptamers selectively isolated hGBM cells with high specificity. EGFR overexpressing tumor cells, when bound to aptamer functionalized surfaces, showed distinct morphological patterns and enhanced activity in contrast to healthy cells, which remained inactive. Tumor cells showed clear changes in cell shapes from spherical to semi-elliptical, with very flat orientation, formed pseudopods (possibly to cover much more surface area) and showed rapid growth. A significant difference in the interactions of normal and diseased cells on functionalized surfaces showed the power of this cytological technique. By using appropriate image processing, we have developed an easy, economical and fast method for the detection of cancer cells. It has the potential to serve as an additional modality to support histological findings and to identify tumor cells based on their physical behavior.
Solid State Micropore Device Functionalized for Selective Enumeration of Tumor Cells

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Introduction: Circulating tumor cell (CTC) enumeration is very crucial for early detection of metastatic cancer. We report a label-free device to selectively count CTCs using aptamer-functionalized micropores. A novel aptamer is used that selectively binds to epidermal growth factor receptor (EGFR), which is known to overexpress on many types of cancer cells. This overcomes issues related to antibodies as well, as antibodies frequently show high levels of off-target cross-reactivity and it is challenging to retain their functionality in varying sample conditions.

Aims and Methods: The aim of this work is to detect low number of CTCs from peripheral blood. A three-step microfabrication process is adopted to fabricate micropores. Human glioblastoma (hGBM) samples are passed through single micropore under a bias voltage. The ionic current flowing through pore is measured with a data acquisition system. When a cell passes through the micropore, it creates a pulse in the current profile. Pulses of tumor cells show distinct profile. Aptamer functionalized and non-functionalized bare micropores are used to quantify statistical differences in the pulse profiles.

Results and Conclusions: The data obtained from aptamer functionalized micropore shows clearly distinctive statistics from that measured from its non-functionalized counterpart. The interactions between the anti-EGFR aptamer and the EGFR on the hGBM cell surface depict different translocation behavior. This device can have applications in cell typing as well, as the sensitivity of the device is at single cell level. The concept is inexpensive and doesn’t require any cell tagging. This can have impact on early cancer detection which can improve cancer diagnosis and subsequently can improve mortality rate. It can also provide insights into the interactions of specific cell types with other aptamers.
Introduction:
Advanced robotic limbs are multi-fingered lightweight devices capable of up to 22 degrees of freedom. However, providing users with natural control and feel of such robotic limbs remains a formidable challenge. Peripheral nerves in the residual limbs of amputees, offers a readily accessible portal to the bidirectional flow of information between the nervous system of the user (motor), and smart robotic prosthetic devices (sensory). To access such portal, several types of peripheral nerve interfaces (PNI) have been developed along a spectrum of invasiveness and sensitivity. We have reported enhanced sensitivity in single spike recordings using carbon nano tube (CNT) coated electrodes for acute brain implantation.

Aims and Methods:
Despite significant advantages of increased surface area and decreased impedance by CNTs, long-term reliability in the recording of such electrodes has not been investigated. Here, we show recording of peripheral nerve activity with CNT coated multi-electrode arrays in freely moving rats. We implanted adult Lewis rats with electrodeposited CNTs on 16 pin Pt electrode arrays placed in the regenerative path of transected sciatic/tibial nerve, using 7/5 mm collagen-filled polyurethane tubes. Neural activity was recorded over time and changes in signal quality were quantified. Stimulation of the sciatic nerve via C-REMI to elicit muscle twitch was done and median current threshold values were recorded. Persistent single unit activity was observed in sub chronic nerve implants 30 days post-implantation and regenerated tissue was processed for visualization of various cellular markers specifically those associated with tissue response.

Results and Conclusions:
Preliminary results show comparable tissue response to uncoated multi electrode implants. This study shows for the first time that CNT-coated REMIs can provide enhanced Signal to Noise Ratio, sensitive recordings of single spike activity and reduced stimulation thresholds in regenerative peripheral nerve interfaces for sub chronic implantation. Together, this data shows that CNT-REMI electrodes provide a sensitive interface for sub chronic recording of single spike activity and safe stimulation of regenerated axons.
Three-dimensional imaging model for studying drug distribution in eyes

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1. Introduction
Many drug releasing particles have been developed for treating posterior ocular diseases. The efficacy of particle drug delivery is hard to assess using either histological evaluation or current imaging modality (MRI and CT) due to poor resolution. There is a need for the development of new method for studying ocular drug delivery with enhanced resolution and sensitivities.

2. Aims and Methods
We developed a 3D imaging model which provides quantitative information about drug distribution in the eye by compiling tissue section scanned images of tissue sections. Briefly, after injected intravitreally injection of with fluorescein (FITC) - a model drug – for different periods of time, the eyes were recovered and frozen sectioned. The tissue sections were imaged using a microarray scanner and processed to produce both 2D quantification results and 3D visualization models using MATLAB® program.

3. Results and Conclusions
The 3D reconstruction starts with removing image artifact and distortion due to histological sectioning method. First, the ocular tissues were rotated and aligned based on the locations of iris, and then corrected using radial basis function. The 2D tissue section 2D images were then compiled into 3D images using MATLAB® program. By comparing the drug distribution at different time points, we found that the fluorescence intensity at the trabecular meshwork and nearby optical nerves were significantly higher at day 2. On day 4, the ocular tissue associated fluorescence intensity was substantially reduced suggesting that most of the injected drugs disappear from posterior chamber. 3D image results also show that most drugs accumulated at trabecular mesh before exiting the ocular tissue. This combined visualization and quantification models allows us to obtain important information for the rational design of drugs or their delivery devices with improved tissue retention and targeting properties.
Dual-responsive poly(N-isopropylacrylamide-acrylamide-chitosan)-coated iron oxide magnetic nanoparticles for controlled and targeted drug delivery applications

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Introduction
Temperature-responsive poly(N-isopropylacrylamide) (PNIPAAm) is commonly used due to its sharp and reversible phase transition at lower critical solution temperatures (LCST, 32-34°C). Hydrophilic acrylamide (AAm) copolymerized with PNIPAAm increases the LCST above 37°C, allowing controlled drug release in vivo. However, non-degradability of PNIPAAm limits its use. This drawback can be overcome by grafting a degradable pH-sensitive polymer, such as chitosan to PNIPAAm, making the structure degradable. Iron oxide MNPs were also incorporated, owing to their applications in magnetic targeting, MRI contrast agents and hyperthermia. Further, particles were conjugated with R11 peptides to obtain R11-PNIPAAm-AAm-chitosan(PAC)-magnetic nanoparticles(MNPs), R11-PAC-MNPs specifically targeted to prostate and loaded with the anticancer drug Doxorubicin, enabling targeted dual responsive drug release and hyperthermia for prostate cancer management.

Aims and Methods
The aim of this study was to synthesize R11-PAC-MNPs for controlled and targeted drug delivery. Particles were prepared by free radical emulsion polymerization. PAC was characterized by FTIR and LCST evaluated by spectrophotometry. Moreover, characterization of PAC-MNPs for size and morphology was performed by dynamic light scattering and TEM. Magnetic properties were analyzed using a vibrating sample magnetometer. Further, drug release profiles were obtained at 25, 40°C and pH 6, 7.4. Finally, cytotoxicity of particles was evaluated on fibroblasts and HPV-7 cells, while cellular uptake of these nanoparticles was studied on PC3-ml.

Results and Conclusions
FTIR confirmed successful formation of PAC on MNPs, whereas VSM studies validated that the coating does not affect its superparamagnetic properties. DLS measurement on PAC-MNPs revealed an average size of 226nm. In addition, cytotoxicity with HDFs and HPV-7 cells showed viability greater than 80% over 24 hours with PAC-MNPs and R11-PAC-MNPs up to a concentration of 500µg/ml. Furthermore, uptake of particles by PC3-ml cells was increased with increasing particle concentration and presence of magnetic field. Thus, R11-PAC-MNPs were successfully synthesized and characterized possessing high cytocompatibility and dual responsiveness. Future studies include in vitro and in vivo testing of these nanoparticles for their effectiveness to detect and treat prostate cancer.
Thermo sensitive fluorescent polymeric theranostic nanoparticles for cancer treatment.

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INTRODUCTION
Thermo-responsive or “smart” polymers can be used for various biomedical applications including drug delivery, tissue engineering and biofunctional molecular techniques due to their phase-transition behavior at or above the physiological temperature to release the loaded therapeutic reagents in response to changes in temperature. The objective of this research is to develop novel biodegradable fluorescent temperature-responsive polymer nanoparticles for drug delivery and imaging applications. Poly(N-vinyl caprolactam) (PNVCL), a thermosensitive polymer is selected as it has better biodegradability and biocompatibility compared to the commonly used thermo-responsive polymer Poly(N-isopropylacrylamide) (PNIPAm). In addition, WBPLP (water soluble biodegradable photoluminescent polymer) is used due to its fluorescent stability, biodegradability, and biocompatibility. Hence in this project, fluorescent thermo-sensitive copolymer PNVCL-WBPLP nanoparticles were synthesized and characterized for both imaging and drug delivery applications for tumor management.

METHOD
WBPLP-PNVCL nanoparticles were formulated via both carbodiimide chemistry and free radical polymerization methods. The size and charge of WBPLP-PNVCL nanoparticles were measured using Dynamic Light Scattering (DLS) technique. In addition, Fourier transform infrared spectroscopy (FT-IR) was done to determine the functional groups and confirm the success of synthesis. The fluorescent spectra were obtained using the UV-Vis spectrophotometer. The LCST (Lower critical solution temperature) was determined using an UV-Vis spectrophotometer coupled with a temperature sensitive probe. The cytotoxicity studies were conducted using the MTS cell viability assay on 3T3 fibroblast cells exposed to these nanoparticles for 24 hours.

RESULTS
Formulated WBPLP-PNVCL nanoparticles have an average diameter size of 200nm using DLS. It was also observed that with a decrease in the PNVCL concentration the LCST increased and vice versa, allowing us to efficiently control LCST of the copolymer according to the choice of application. An LCST of 450°C was optimized for further studies as it’s an ideal temperature for hyperthermia therapy. The cytotoxicity results show more than 80% cell viability for up to 500µg/ml concentration of nanoparticles, suggesting these nanoparticles are biocompatible. In vitro drug release studies are being performed over 21 days using doxorubicin as an anti-cancer drug model. Future work includes in vivo studies to investigate the fluorescent imaging, biodistribution, and effectiveness of these nanoparticles for cancer diagnosis and therapy.
Efficacy of NU7441-encapsulated PLGA nanoparticles in radiation sensitization of prostate cancer cells

Jyothi U. Menon, Vasu Tumati, Jer-Tsong Hsieh, Kytaí T. Nguyen, Debabrata Saha

Introduction: Prostate cancer remains the leading cause of cancer-related mortality in men with an estimated 241,740 new cases and 28,170 deaths expected by end of 2012. Conventional cancer treatments such as radiation therapy can be ineffective due to radiation resistance of prostate cancer cells. This resistance arises due to their increased DNA double strand break (DSB) repair ability, especially through Non-Homologous End Joining (NHEJ). In this study, we have developed biodegradable and biocompatible poly lactic-co-glycolic acid (PLGA)-based nanoparticles containing the potent radiosensitizer NU7441 (8-dibenzothiophen-4-yl-2-morpholin-4-yl-chromen-4-one) for radiation sensitization of prostate cancer cells by inhibiting DNA-dependent protein kinase, which regulates NHEJ.

Aims and Methods: PLGA nanoparticles encapsulating NU7441 and iron oxide as an imaging and targeting agent were prepared by a standard double emulsion technique and characterized for size and surface charge. R11 peptide was surface conjugated onto the nanoparticles for prostate cancer-specific targeting. Stability studies in de-ionized (DI) water and serum were conducted over 5 days followed by drug release studies in DI water at 37oC. Further, in vitro studies were done to study cytocompatibility with health prostate cells (PZ-HPV7) and cellular uptake by prostate cancer cells (PC3). DSB repair kinetics of prostate cancer cells following nanoparticle uptake was studied using a DSB repair assay.

Results and Conclusions: Our nanoparticles had an average size of 274.13 ± 79.96 nm and showed good stability in water and serum for 5 days. The nanoparticles also showed bi-phasic NU7441 release within 21 days at 37oC and >80% PZ-HPV7 cell viability up to 2000 µg/ml nanoparticle concentration. Further, the particles were selectively uptake by PC3 cells in a dose and magnetic field-dependent manner and showed effective radiation sensitization of these cells in vitro. Our results thus demonstrate that R11-conjugated PLGA-iron oxide nanoparticles containing NU7441 are biocompatible and can be potentially used to radiosensitize prostate cancer cells in vivo.
Brain Controlled Prosthetics: Towards a Functional Near-Infrared Spectroscopy (fNIRS)-Finger Interface

Matthew Cooley, Adithya Ganesh, Eric Musselman, Jackson Schad, Duncan MacFarlane

8,000 finger, wrist, and hand amputations occur per year in the U.S. alone.[1] Partial hand injuries account for approximately 1/3 of chronic occupational injuries, 1/4 of lost working time, and 1/5 of permanent occupational disability.[2] Meanwhile, there are few functional (non-aesthetic) single-finger prostheses in the commercial space; the authors found 2. The authors aim to create a lightweight functional prosthetic finger that can perform precise tasks particularly for touchscreen applications.

A model prosthetic finger was designed through the 3D CAD program SolidWorks, and printed using a Dimension 3D Printer. The prosthetic has a hexagonal body shape for rigidity and a high strength-weight ratio. The prosthetic is capable of activating touch screens through a charged aluminum foil probe connected to a voltage source to activate the screen’s capacitor. An Atmel ATTiny 85 microcontroller powered by a watch battery runs a C program that controls Spektrum 2.3g micro servo-motors. This architecture fits entirely within the finger. On a touch interface, the single-finger prosthetic is capable of texting, phone dialing, navigating the web, and playing the piano.

Recorded fNIRS data from a finger-tapping protocol was used as a control signal to activate the prosthetic. Adapted from Khan et al.[3][4], various digital signal processing techniques, were implemented in MATLAB to analyze this data and filter noise, partially through HomER (Hemodynamic Evoked Response), an open-source MATLAB package. Band-pass filtration was employed to filter noise outside of the signal’s own frequency range. Principal component analysis was used to remove noisy eigenvectors through an eigendecomposition of the covariance matrix. The least-mean-squares gradient descent adaptive filter was then utilized to remove the remaining residual noise. A normalized cross-correlation metric, smoothing low-pass filter, and derivative impulse threshold, were collectively used to correlate changes in levels of HbO and HbR with digit movement that motor cortex brain activity controlled.

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Biomechanical Testing of Pelvic Organ Prolapse Tissue for Modeling towards Corrective Mesh Design

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Introduction

Synthetic meshes used in pelvic organ prolapse corrective surgery are becoming increasingly problematic, resulting in adverse side effects such as pain, infections, and discomfort. The implanted meshes slowly shear away and erode through the tissue, as they are too tough and not biodegradable. This is due to a mismatch between material and tissue mechanical properties. Biomechanical testing of human tissue is essential for the accurate modeling of human vaginal tissue and results in better understanding of structure and function, especially in prolapse states. These models can be used to inform material selection for corrective mesh design.

Aims and Methods

Vaginal tissue samples are harvested from cadavers or from patients in the operating room; these are frozen and then thawed before analysis. In this study, we have begun measuring shear strain of much smaller fresh tissue samples using dynamic mechanical analysis (DMA). We obtain biaxial data that better depict the viscoelastic properties of tissue. The lower frequencies examined imitate pelvic straining efforts better than higher strains of our previous studies. Biaxial measurements were attained by running tests on the sample in longitudinal and transversal orientations. Frequency sweeps of 100Hz to 0.1Hz were run on samples at constant 37 °C temperature. This novel approach to biomechanical testing of human tissue is necessary to design superior models of tissue and develop improved corrective meshes with clinical relevance.

Results and Conclusions

We have found that vaginal tissue displays different levels of anisotropy in non-prolapsed and prolapsed states. We have also begun investigating the effect of freezing on tissue. The collected data will be used to inform constitutive hyperelastic models of tissue response to strain. Material investigation is well under way to determine a bioresorbable polymer that is mechanically compatible with tissue.
As the approach to medicine shifts from corrective to preventive care, the need to monitor patients on a continuous basis becomes necessary in order to cope with the growing number of people who are at risk of suffering chronic illnesses. Telemedicine, defined as the remote monitoring of an individual’s vital signs and other health-related information, addresses this need.

In 2010 the National Health Expenditure reached $2.6 trillion and is expected to have grown by 5.5% this year. Approximately seventy-five percent of the money was spent on the prevention and cure of preventable diseases. Using telemedicine, a doctor can identify an ailment in its early stage and suggest an action plan that may prevent the disease from fully manifesting itself. By preventing disease, the use of telemedicine decreases the strain on the economy by reducing costs to patients as well as tax payers. More importantly, preventing a disease raises the quality of life enjoyed by the individual. Due to the importance of such a system to the health of an individual, the system must be robust and dependable. The system may be used to monitor anyone including individuals in a senior care center to athletes on a football field to elementary school students. My investigation identifies the necessary components of a feasible and robust telemedicine system as well as analyzes its effects on the end-users (patients, doctors, emergency responders, insurance companies, etc.). The HealthPortal system comprises of biosensors, the PatientPortal software, a secure website, the PersonnelPortal software (for healthcare providers), and software for clinics, hospitals, insurance companies and health agencies.

The goal is to integrate these roles through the software which will bring about improved communication and therefore improved outcomes in terms of both finances and wellbeing.
Using Sparse Sensors for In-shoe Plantar Pressure Monitoring
Sarah Ostadabbas, Mehrdad Nourani

INTRODUCTION—The foot complications constitute a tremendous challenge for diabetic patients, caregivers, and the healthcare system. With current technology, in-shoe monitoring systems can be implemented to continuously monitor foot’s at-risk ulceration sites and send feedback to patients and physicians.

AIMS AND METHODS—Several in-shoe monitoring systems, reported in literature, depend on pressure sensors placed precisely at the pressure points. There are three key shortcomings in this method: a) the pressure sensors have to be uniquely placed for each subject, b) small misplacement greatly affects accuracy, and c) there is no good way to estimate pressure on other points on the foot. In this work, we model the foot’s pressure distribution by using a method that depends on a small number of sensors, called Sparse sensing Continuous Plantar pressure Model (SCPM). This model uses a modified Gaussian Mixture Model (GMM) to reconstruct a continuous plantar pressure map. In the SCPM, each pressure point is represented by one or more Gaussian functions. The number of Gaussian functions, their centers, and their covariances (shapes) are trained using data from a high-resolution pressure mapping system.

RESULTS—In order to collect pressure data for SCPM training, we designed and assembled our own smart insole with sensors and data collection/processing capabilities. For training, we used the MatScan pressure measurement system. In training phase, five healthy subjects were asked to walk on a high-resolution pressure mat and the pressure data was used to create an accurate foot pressure model of each subject. The impact of various metrics on the accuracy of data reconstruction was evaluated for different number of basis functions and pressure sensors.

CONCLUSIONS—Our proposed SCPM takes advantage of high-resolution pressure data during training to create an accurate pressure model of the subject's foot. Subsequently, only a small number of sensors is required to estimate pressure anywhere on the foot. Furthermore, the sensors do not need to be placed on exact peak pressure spots to generate an accurate map. This allows production of generic sensor insoles rather than the per-subject customization required in other methods.
3-Dimensional Assessment of In Vivo Corneal Wound Healing using a Modified HRT-RCM Confocal Microscope

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Background: Confocal microscopy is ideally suited for studying corneal wound healing in vivo. The recently developed HRT Rostock Corneal Module (HRT-RCM) provides excellent resolution, contrast and optical sectioning capability – defining features of confocal microscopy. However, changing the focal plane over large distances requires rotating the thumbscrew objective housing by hand, which limits the ability to perform quantitative 3-D imaging.

Purpose and Methods: The purpose of this research was to develop and test both hardware and software modifications for the HRT-RCM to allow quantitative 3-D corneal scanning. To automate the HRT-RCM focusing mechanism, a PC-controlled rotational stepper motor drive was attached to the microscope housing. To test the system for quantitative imaging, rabbit corneas were scanned both before and 1, 3, 7 and 14 days after transcorneal freeze injury (FI), which damages all corneal cell layers. Continuous scans were made from the endothelium to the epithelium at a constant lens speed, while collecting images at a rate of 30 frames/second. Image sequences were read into a custom-developed program for depth calculation and measurement of sub-layer thicknesses. Estimates of corneal backscattering were obtained by measuring the area under intensity vs. depth curves.

Results and Conclusions: Following freeze injury, a significant increase in both corneal thickness and light scattering was measured, due to tissue edema. Prior to surgery, corneal stromal cells (keratocytes) maintain a quiescent, dendritic morphology. However, from 7 – 14 days after FI, keratocytes repopulating the damaged tissue assumed an elongated and interconnected fibroblastic morphology, and a dramatic increase in cellular light scattering was measured. Overall, this modified system provides high resolution 3-D image stacks from the full thickness rabbit cornea in vivo. These datasets can be used for interactive visualization of corneal cell layers, measurement of sub-layer thickness, and estimation of stromal backscatter (haze) during wound healing.
A Novel Microwave Radiator Structure for Non-invasive Breast Cancer Detection
Arezoo Modiri, and Kamran Kiasaleh

Introduction:

Microwave Imaging has been investigated for years and it is claimed to be a promising technique for breast cancer detection. Here we introduce a novel radiator structure and demonstrate its detection results in simulation and experiment.

Aims and Methods:

A practically implementable structure and its quite encouraging detection results for breast cancer are shown in this study. The novelty of the proposed structure, as compared to its counterparts introduced in the literature resides in its interesting potential as a self-examine detector. The ultimate goal is that the patients use the device themselves with no need to any physical presence in a clinic. The device should be used periodically for routine checkups. It is designed to compare the current situation of the tissue with the built-in history of the previous measurements, and to detect the changes which may actually be due to a tumor creation even at its early stages. For our measurements, we used an ENA and the measured data was analyzed in MATLAB to generate the cumulative differences in phase and magnitude of the scattering parameters between normal and cancer tissues. The simulations were done in HFSS.

Results and Conclusions:

The preliminary simulation and experimental results of our novel radiator structure are promising. In the simulations, Ansoft digital human phantom was used in order to have a precise model of female body. The tool could detect the tumors in different shapes and sizes up to the depth of 4cm. For our preliminary experiments, we built two breast phantoms, one of which had a donated breast tumor inside it. The tumor was placed inside the glandular tissue at the depth of almost 4cm. It was shown that measuring the S parameters and calculating the cumulative differences, one can successfully identify the existence of an abnormality in the cancerous phantom.
Online Calibration of Interface Characteristic Variation in Capacitively Coupled Non-Contact EEG Acquisition System

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Gel-free, non-contact electroencephalograph (EEG) acquisition is quickly arising as a contender to conventional wet-electrode sensing techniques, particularly for ambulance applications. One critical problem in non-contact EEG system is the characteristic or impedance variation of the capacitively coupled scalp-electrode interface (SEI) due to head movement, eye blinking, or muscle activities. Such variation poses significant challenges to the coupling-gain stability of the recording analog front-end (AFE) and if uncorrected may cause severe signal distortions.

Recently, active grounding and contact impedance monitoring techniques are reported to alleviate the interface stability issues. However, the former technique is aiming at common-mode noise rejection while the latter does not constitute any correction to the recorded signal. In this work, an in-situ SEI gain adaptive calibration technique is presented, which utilizes a test-signal injection through the existing active-grounding amplifier to track the time-varying gain (while allowing simultaneous EEG recording) and subsequently corrects the recording for any gain errors in the digital domain. The time-dependent gain is identified through a background digital cross-correlation process and corrected individually for each electrode in the system.

An experimental EEG system is built using low-cost passive electrodes and TI ADS1298 biomedical acquisition board. A 2-kHz, 1-mV square wave is injected through the driven right leg (DRL) circuit on ADS1298 to a reference electrode anchored behind the ear and picked up by the electrodes placed on the scalp. P300 spelling test was conducted and the recording lasted for 29 seconds. During the recording, the subject was instructed to freely move his head around to aggravate the SEI coupling condition. The cross-coherence between two EEG components after independent component analysis (ICA) was calculated to be 6.0% and 87.1% without and with calibration, respectively, in this case. The improvement was obtained without any time-domain averaging on the raw data to improve SNR.
Synergistic Axonal Growth from Postnatal Spinal Cord Explants by Brain-Derived Neurotropic Factor and Pleiotrophin Combinatorial Treatment

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Introduction

The lack of spontaneous regeneration in the adult spinal cord often results in permanent sensory motor impairments after injury. Application of neurotropic factors, blocking myelin-associated inhibitors, and enzymatic degradation of the proteoglycan-based glial scar are have been shown to elicit some axonal regeneration across the injured spinal cord. Specifically, several growth factors such as brain-derived growth factor (BDNF), glial-derived nerve factor (GDNF) and pleiotrophin (PTN) have been demonstrated to induce axonal growth in the injured spinal cord. However, whether these factors have differential neurotropic potency, or whether their combinatorial treatment would confer specific regenerative advantage over any single growth factor treatment, remains to be determined.

Aims and Methods

Here we systematically evaluated the differential effect of BDNF, GDNF and PTN, alone or in combination, on their ability to induced axonal regeneration in dorsal root ganglion sensory neurons and spinal cord explants cultures. Number of axons, total neurite length, and number of axonal branches will be quantified in each of these groups.

Results

Our results indicate that PTN induces 50% increase in axonal length and is more potent than BDNF or GDNF. However, a PTN/BDNF combination doubled the amount of axonal growth observed from spinal cord explants to approximately 300% compared to either growth factor alone, while GDNF did not seem to contribute significantly in enhancing axon regeneration. The synergistic effect is most evident in the axonal length in spinal cord sections and axonal density in DRG. We are currently investigating the cellular and molecular mechanisms that underlie the observed synergistic effect of neurtrophins and pleiotrophins in the spinal cord. Our results will contribute towards the elucidation of the most effective trophic support needed to entice nerve regeneration in the injured spinal cord.
Regenerative Multi-electrode interfacing of the tibial nerve

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INTRODUCTION: Providing natural control of movement and feel to the users of advanced robotic prosthetics remains a formidable challenge. Electrode arrays implanted into peripheral nerves have demonstrated the ability to both sense neural activity and elicit sensations after stimulation of the interfaced nerve fibers. However, current peripheral neural interfaces are not specific for sensory stimulation or capable of recording exclusively from motor activity. We have previously reported a regenerative multi-electrode interface (REMI) that can record from mixed sensory-motor nerves in the peripheral nervous system, and that neurotrophic factors can be used to entice the specific regeneration of modality-specific axons. Here, we evaluated the level of neural activity recorded from naturally segregated motor nerves during resting, random or stereotypic locomotion.

METHODS: Lewis rats received REMI implants into the tibial motor nerve. Using gait and kinematic analysis 30-60 days after implantation, we confirmed that kinematic parameters of the regenerated interfaced tibial nerve were comparable to uninjured animals. Then, the recorded neural activity from the tibial-REMI from fully alert animals was positively correlated with EMG activity and gait analysis evaluated during treadmill locomotion.

RESULTS AND CONCLUSIONS:

- Chronic regenerative interfacing of a tibial nerve does not significantly alter max step height during bipedal locomotion.
- We demonstrated coordinated burst activity between some electrodes and EMG activity.
- Based on firing rate some electrodes seem to correlate well with EMG activity suggesting they are likely to be motor units.
- We also observed neurons that do not correlate with gait or EMG, but rather show tonic activity which is highly indicative of proprioceptive activity.
- We have identified individual single units according to functional subtype based on the correlation of muscle activity.
**In vivo** metabolic imaging in human brain tumors using magnetic resonance spectroscopy

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**Introduction:**

Magnetic resonance spectroscopy (MRS) allows non-invasive measurement of metabolites *in vivo*. However, its integration into oncological clinical practice has been limited due to difficulties in measuring low concentration metabolically important metabolites. In recent years, several seminal studies have shown changes in the metabolic pathways in brain tumors driven by oncogenic mutations and hypothesize that blocking these pathways can suppress tumor growth. Studies also showed that metabolic changes occur before morphological changes, hence robust, reliable and quantitative MRS techniques are needed to investigate such changes non-invasively. We developed techniques for measuring glutamate, glutamine, 2-hydroxyglutarate (2HG), glycine and other brain metabolites *in vivo*. We performed experiments on healthy volunteers and subjects with various WHO grades brain tumors.

**Aims and Methods**

We performed numerical simulations of standard point-resolved spectroscopy MRS sequence to improve detectability and differentiability of difficulty to measure metabolite signals. These simulations lead to discovery of optimal scanning parameters for detection of aforementioned metabolites. For example, an echo time of 97 ms was optimal for detection of 2HG, Glu, and Gln and an echo time of 160 ms was optimal for detection of glycine. These optimized parameters were validated in experiments performed on phantoms and healthy volunteers on a 3T whole-body Philips MR scanner. Pre- and post-chemotherapy and radiation treatment scans were carried out in many patients to monitor the changes of metabolites levels over the course of the treatment.

**Results and Conclusions**

- We have detected, for the first time, elevated 2-hydroxyglutarate levels in brain gliomas with IDH mutations. Our technique showed cent-percent correlation with the tumor histo-pathological (biopsy) results in detecting IDH mutations. In many patients the levels of 2HG in the tumor correlated with the clinical symptoms (mostly seizures)
- We detected elevated levels of glycine in some high grade (glioblastoma multiforme, GBM) patients
- Most subjects showed elevated glutamine and reduced glutamate, indicating a significant change in the energy metabolism of the tumor cells

Our present work demonstrates the viability of developed techniques for *in-vivo* measurement of brain metabolites, which can be implemented on clinical MR scanners.
A Hardware-Software Solution for Pressure Ulcer Prevention
Masoud Farshbaf, Rasoul Yousefi, Sarah Ostadabbas, Mehrdad Nourani

INTRODUCTION: Pressure ulcers are imposing a huge cost on our healthcare system. Pressure of bony parts against soft tissues is the main factor contributing in formation of pressure ulcers. Several pressure mapping systems are available that produce real-time pressure image. However, there is an increasing need for a hardware-software platform with embedded signal processing algorithms to analyze captured pressure images using pressure sensors and provide medically meaningful feedbacks to the caregivers.

AIMS & METHODS: The purpose of this study is to develop an analytic that capture the interface pressure between patient’s body and support surface in real-time and analyzes the interface pressure in order to identify at-risk postures and body zones of bed-bounded patients such as sacrum, back and heel. The at-risk zones are automatically tracked and their corresponding pressure statistics are monitored and properly visualized to assist nurses in providing an effective care to the patients. A commercial pressure mapping system is used on the hospital bed to capture the interface pressure. The quality of pressure image is then enhanced using image processing techniques including nonlinear digital filtering. A binary pressure image is created based on which a limited number of stable postures are extracted. For each frame and each posture, and depending on the patient’s weight and body structure, a Center of Pressure (COP) is located and the scatter plot of location of the COP is extracted. Finally, a clustering algorithm is applied on the scatter plot and the final centroid location of the clustering algorithm is scored based on the number of the points in corresponding cluster. Clusters with large number of points are used to identify the high-risk zones which will be automatically monitored and marked for caregivers’ attention on the monitoring tool.

RESULTS & CONCLUSION: Several hours of pressure image from five subjects between ages of 18-50 years old are collected and the algorithm is validated by analyzing the collected data. The developed software is able to transfer visual representation of the pressure map and at-risk body zones/postures to caregivers’ monitoring station. We have developed tools and algorithms that are able to work with available pressure mapping systems and analyze pressure maps in order to provide feedback to caregivers. This platform can significantly assist in monitoring and prevention of pressure ulcers. Monitoring at-risk regions and positions can be combined with traditional turning (e.g. 2-hour) policy to achieve a much more effective care and results.
Detection of Ex-Vivo Breast Cancer Positive Margins using Hyperspectral Imaging

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Scope: Current intra-operative detection of breast cancer margin of lumpectomies is performed visually by surgeons. However, it is reported that 30-50% of positive margins are missed requiring a further surgery to remove the remaining cancer. To improve the detection of positive breast cancer margins during surgery, the use of hyperspectral imaging is examined in this study.

Hyperspectral Imaging System: The utilized hyperspectral imaging system has a micro-mirror-based DLP (digital light processor) which illuminates a tissue sample at 101 individual wavelengths between 370 nm and 780 nm in time sequence within one minute. Incident light is reflected off the specimen and then detected by a CCD camera. In other words, a 101-wavelength spectrum or hyperspectral data is obtained at each pixel, reflecting the absorption and scattering characteristics corresponding to that pixel region. For this study, the reflectance signals of known breast tissue types that had been labeled using their histology classification were analyzed.

Detection Study and Results: A detection study was conducted based on 19 breast cancer tissue specimens from which 14 cancerous, 17 adipose, and 16 fibrous regions-of-interest were extracted. The reflectance signals corresponding to a total of 2928 cancerous pixels, 4321 adipose pixels and 3425 fibrous pixels in these regions were used to form our analysis samples. The samples of adipose and fibrous reflectance signals were combined to form a non-cancerous class. A total of 2000 reflectance signal samples were selected randomly from the cancerous and non-cancerous classes to train five different classifiers and the rest of the samples were used for testing the classifiers. The training and testing were repeated 10 times, each time selecting different sets of training and testing samples. Among the classifiers examined, the 3rd-order polynomial SVM (support vector machine) classifier generated the best classification outcome resulting in 98.09% sensitivity and 99.35% specificity. These results demonstrate the potential of using hyperspectral imaging to improve the detection of positive breast cancer margins.
Multiluminal Biosynthetic Repair of Long-Gap Peripheral Nerve Injuries

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Introduction – Peripheral nerve injuries can be repaired with engineered therapeutics, but in cases of axotomy from trauma or clinically-induced injury longer than a short gap, the results are varied. Here we present the results of polymer, drug delivery, and growth factor research to bridge clinically challenging distances with conduits. Autografts remain the treatment of choice for nerve defects despite the need for donor nerve harvesting and the associated morbidity of this procedure. Despite success in short gap injuries, isografts achieve sub-normal functional recovery for gaps longer than a critical 30 mm length, and simple tubularization methods fail completely. The regenerative failure of peripheral nerves through long gaps can be attributed to the lack of both appropriate growth substrate and trophic support. With long gap repairs we decided to approximate endoneural structure in a multiluminal conduit. Further, we reasoned that successful nerve regeneration across long-gap nerve defects would require growth factor support and early vascularization.

Aims and Methods – Vascular endothelial growth factor (VEGF) and Pleiotrophin (PTN) have growth promoting effects on broad cellular targets including neurons, Schwann cells and endothelial cells. Our team incorporated encapsulated growth factors into our multiluminal 30-mm nerve conduit. This conduit was tested in New Zealand White rabbits. In five groups, with 33 total animals, we tested the following: a hollow tube with collagen, a BNI conduit, a BNI conduit with VEGF, a BNI conduit with PTN, and a BNI conduit with both VEGF and PTN. Nerve conduction, histology, and behavioral testing were used to compare regeneration and functional recovery.

Results and Conclusions – Here we report the substantial benefit of a multi-luminal nerve implant for repair across critical peripheral nerve gaps. Further, the results of this study support the notion that broad growth factor support enhances nerve repair and functional recovery in long-gap nerve lesions.
Speech Recognition for Patients with Dysarthria Related Symptoms

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Speech is one of the most natural and intuitive means of communication for humans. Dysarthria is a neuromuscular disease that can hinder the proper operation of the vocal tract muscles. It can be caused amongst others by stroke, trauma or cerebral palsy. Its symptoms include paralysis, reduced range of motion and poor coordination of the muscles of the oral cavity, thus limiting the ability to produce articulatory gestures. These symptoms can hamper the accuracy of an automatic speech recognition system when attempting to transcribe speech from a patient with this condition.

In order to overcome the difficulties posed, we developed a novel speech recognition system that in addition to audio signals, it utilizes visual information to compensate for speech disorders. More specifically, our system utilizes planar video as well as 3D information of the speaker's mouth captured by a Kinect sensor. These additional streams constitute an additional modality containing meaningful speech information that is temporally correlated to the audio signal.

We conducted extensive experiments in order to examine the accuracy and robustness of our system in comparison to a traditional audio-only speech recognition system. More specifically, we mixed the audio signal with babble noise at various SNR levels in order to simulate slurred speech due to affected muscles of the vocal tract. In addition, we degraded the quality of the visual information by occluding particular areas of the speaker's mouth in order to simulate paralysis of the lip muscles. The word recognition accuracy that our system achieved for slurred speech was higher by 20.37% on average than an audio-only system. In the case of both affected speech and lip movements, our system achieved an absolute average increase in of 10.14%. In conclusion, we developed a novel system that utilizes visual information for speech recognition and is able to attain higher performance than traditional systems.
Biodegradable thermo-responsive nanoparticles

Damanpreet Kaur, Jyothi U. Menon, Kyta Truong Nguyen

Introduction

Stimuli-sensitive materials which can alter their conformation and properties, in response to changes in physiological variables, are receiving increasing attention as therapeutic devices. Temperature sensitivity is an interesting property of stimuli-responsive polymers. Thermo-responsive polymers that undergo reversible phase transitions at a certain temperature show potential for drug delivery systems to release loaded drug in response to changes in temperature. These polymers swell below and collapse above lower critical solution temperature (LCST), thereby triggering drug release. Poly(N-isopropylacrylamide) (PNIPAm) is the most studied thermo-responsive polymer, and it exhibits LCST at 32°C. The main disadvantage of PNIPAm is its non-biodegradable nature, which limits its use in biomedical applications. Methyl cellulose is thermo-responsive biodegradable polymer, with LCST of 50°C–60°C, which is higher than physiological and/or ideal hyperthermia temperatures. In this study, we have prepared novel methyl cellulose(MC)-acrylic acid(AAc) nanoparticles with lower LCST and investigated their efficacy in drug delivery applications.

Preparation and characterization of nanoparticles

The nanoparticle formulation of MC and AAc copolymer was performed by free-radical reaction using ammonium persulfate and N,N,N',N'-tetramethylethylenediamine. Nanoparticle size and charge were measured by dynamic light scattering (DLS) and zeta potential analyzer. Particle morphology was observed using Transmission electron microscopy (TEM). LCST measurements were taken by differential scanning calorimetry and by measuring optical transmittance of polymer solution using UV–vis spectrometer. The Fourier transform infrared spectroscopy (FTIR) analyses of nanoparticles were done to determine functional groups of these nanoparticles and success of copolymerization.

Results

The MC-AAc nanoparticles had an average size of 250 nm and zeta potential of -14.89 mV. LCST was observed at around 40-45°C indicating that these particles could be used to incorporate metal-based components in the future to potentially induce hyperthermia and subsequent drug release for cancer applications. Our FTIR results confirmed the successful copolymerization of MC with AAc. In vitro and in vivo studies will be conducted in the future to investigate the biocompatibility and potential use of these nanoparticles for drug delivery and other biomedical applications.
Top-Down Analysis of Intact Proteins by Superficially Porous Liquid Chromatography Coupled to High-Resolution Mass Spectrometry for Biomarker Discovery

Daniel A. Plymire, Junmei Zhang, Michael J. Roth, Erica M. Maresh, John C. Corbett and Steven M. Patrie

Introduction

Multiple Sclerosis (MScl) is a disease of the central nervous system characterized by sclerotic plaques and autoimmune response. Improved diagnostics and biomarker discovery has the potential to facilitate earlier treatment, improve diagnosis, and reduce disease progression. Many autoantigens involved in MScl, including myelin basic protein (MBP), are heterogeneous due to alternative splicing and post-translational modifications. Additionally, differences may exist between various glycoproteins present in the cerebrospinal fluid (CSF) of MScl patients.

Our platform including isoelectric focusing (IEF) and superficially porous liquid chromatography (SPLC) for separations, followed by detection by high-resolution mass spectrometry (i.e. top-down proteomics), has been shown to identify the heterogeneity in a number of molecules, including MBP and prostaglandin D synthase (PGDS) and has potential to discover novel biomarkers that may aid in diagnostic and therapeutic development.

Methods

Murine MBP was isolated from brain tissue. Glycoproteins from CSF were separated by IEF. SPLC resin (Agilent) was packed into a PicoFrit LC column (New Objective) in house. The analysis platform included an 1100 nano LC system (Agilent) coupled to a LTQ Orbitrap XL mass spectrometer (ThermoFisher). Nozzle skimmer fragmentation of MBP and PGDS yielded fragment masses that were used for database search with ProSightPC 2.0 (ThermoFisher).

Results

Preliminary SPLC/MS analysis of murine MBP shows that all common splice variants (14-20 kDa) were separated and observed, with many combinations of post-translational modifications. From observation of unique intact masses and knowledge of column peak capacity we estimate that 500-1000 unique 14 kDa MBP species can be observed in single run, potentially allowing correlation between the different MBP isoforms observed and disease state. Visualization of glycosylation patterns from CSF identified many isoforms of PGDS, a highly abundant protein in CSF. Differential expression of the PGDS glycoforms was observed when comparing patients with MScl to controls, suggesting avenues for the investigation of novel biomarkers.
Introduction
Hydrogels are chemically or physically cross-linked polymer networks that imbibe water and retain their swollen structure in water. The extent of swelling depends on the number of hydrophilic groups in the hydrogel. High water retention makes hydrogels biocompatible, with high drug loading and ECM-mimicking capabilities. Hydrogels are used in a variety of applications like scaffolds for tissue engineering, vehicles for drug delivery, contact lenses, wound dressings, molecular imprinting and so on. In this project we attempted to design an injectable nano-composite system that was made of hydrogel [copolymer of PEGMC: poly(ethylene glycol maleate citrate) and PEGDA: poly(ethylene glycol diacrylate)] and biodegradable polymer [PLGA: poly(lactic-co-glycolic acid)] nanoparticles. The anticancer drugs 5FU (5-FluoroUracil) and curcumin were loaded into hydrogel matrix and PLGA nanoparticles, respectively, to overcome multidrug resistance and also deliver comparatively higher dosages of drug to the tumor site than systemic drug delivery methods.

Aim and Method
The aim of this project was to develop an injectable hydrogel – nanoparticle composite system for dual drug delivery to local tumor site. The PLGA nanoparticles were made by single emulsion technique and loaded into chemically cross-linked PEGMC-PEGDA hydrogel. Factorial analysis was performed to optimize the average curing time. The nanoparticles were characterized for their size and morphology. Further, degradation, drug release and swelling ratio studies were done to optimize the hydrogel as an injectable nano-composite system.

Results and Conclusion
The average size of nanoparticles was 249 nm with a drug loading efficiency of 49.43%. The average swelling ratio of the nano-composite system was found out to be 91.548 ± 0.63. The curing time of the optimized run was approximately 3 min. It was also found that by varying the amount of PEGDA and initiator, we could vary the degradation rate of the system. Further in vitro and in vivo studies will be performed to determine the potential use of our hydrogel nanoparticle composite system for local, controlled dual drug delivery to overcome multidrug resistance in specific cancer cells.
Flexible needle insertion planning and implementation for multiple planar targets
Jaeyeon Lee and Wooram Park

Introduction
A long and flexible needle with a bevel tip has great potential as an interesting research topic showing different characteristics against the traditional short and stiff medical needle. A user can generate a curved shape of needle trajectory and control it using two simple inputs: pushing along and rotating around the needle axis. This property consequently allows the user to target desired points by the flexible needle, which can avoid the obstacles and minimize tissue damage in the body during needle insertion.

Aims and Methods
We develop an insertion plan of the flexible needle with multiple targets and a single entry point in 2-D environment. The multiple targets in the plane can be reached by the flexible needle through repetitive actions such as insertion, partial retraction, rotation, and re-insertion of the needle. The planning method finds the optimal entry point and corresponding direction with which we can generate the optimized needle path that can be gained by a geometric relationship between multiple tangent circles. We defined the cost function of the trajectory and numerically solved the minimization problem so that the optimized trajectory can minimize the tissue damage that is estimated by the length of the needle path.

Results and Conclusion
In order to verify the plan, the C#-based software with GUI and the semi-automatic hardware were built to compute the optimal needle paths and perform the planned insertion as an open-loop controller. The experimental results showed that the open-loop controller could insert the needle to target multiple points with the error less than 3mm. The averaged error was less than 2mm. This small error increased the expectation that the needle insertion based on the proposed planner will be very accurate with the feedback controller.
Detection of Ex-Vivo Breast Cancer Positive Margins using Hyperspectral Imaging

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Peter LeBoulluec, Hanli Liu (University of Texas at Arlington)
Yan Peng, David Euhus (University of Texas Southwestern Medical Center)

Scope: Current intra-operative detection of breast cancer margin of lumpectomies is performed visually by surgeons. However, it is reported that 30-50% of positive margins are missed requiring a further surgery to remove the remaining cancer. To improve the detection of positive breast cancer margins during surgery, the use of hyperspectral imaging is examined in this study.

Hyperspectral Imaging System: The utilized hyperspectral imaging system has a micro-mirror-based DLP (digital light processor) which illuminates a tissue sample at 101 individual wavelengths between 370 nm and 780 nm in time sequence within one minute. Incident light is reflected off the specimen and then detected by a CCD camera. In other words, a 101-wavelength spectrum or hyperspectral data is obtained at each pixel, reflecting the absorption and scattering characteristics corresponding to that pixel region. For this study, the reflectance signals of known breast tissue types that had been labeled using their histology classification were analyzed.

Detection Study and Results: A detection study was conducted based on 19 breast cancer tissue specimens from which 14 cancerous, 17 adipose, and 16 fibrous regions-of-interest were extracted. The reflectance signals corresponding to a total of 2928 cancerous pixels, 4321 adipose pixels and 3425 fibrous pixels in these regions were used to form our analysis samples. The samples of adipose and fibrous reflectance signals were combined to form a non-cancerous class. A total of 2000 reflectance signal samples were selected randomly from the cancerous and non-cancerous classes to train five different classifiers and the rest of the samples were used for testing the classifiers. The training and testing were repeated 10 times, each time selecting different sets of training and testing samples. Among the classifiers examined, the 3rd-order polynomial SVM (support vector machine) classifier generated the best classification outcome resulting in 98.09% sensitivity and 99.35% specificity. These results demonstrate the potential of using hyperspectral imaging to improve the detection of positive breast cancer margins.
Optimization of novel multifunctional nanoscaffolds for re-endothelialization *in situ*

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Angioplasty and stenting are common treatments for clogged arteries. Drawbacks to these treatments include damage to the arterial wall. Denudation of endothelial tissue allows the deposition of von Willebrand factor (vWF). Binding to vWF activates platelets and subsequently results in thrombosis and restenosis. A novel multifunctional nanoscaffold system for *in situ* re-endothelialization has been developed. The nanoscaffolds were conjugated with dual ligands (GP1b, and anti-CD34). The particles target the sub-endothelial tissue and prevent platelet deposition via GP1b, and recruit endothelial progenitor cells (EPC) from the blood stream via anti-CD34. The goal of this research is to optimize the functionality of this nanoscaffold system. Several factors were manipulated and studied including: particle size (200 nm, 500 nm, 1 µm, and 5 µm), ligand concentration, monolayer deposition and EPC capturing efficacy in order to achieve optimal performance of the particle functionalities. Synthetic microvascular networks (SMN) are microfluidic chambers modeled after native vascular structures. SMN which mimics physiological flow conditions will be used to examine the particle adhesion/deposition. From our results we have concluded the optimal ligand density, based on 200 nm particles to be 50 µg ligand/mg particles. To achieve monolayer coverage, various sizes of particles were incubated with vWF coated substrates. We found that binding of microparticles results in higher surface area coverage as compared to nanoparticles. Future work focuses on studying the effect of particle sizes to vascular injury targeting at various shear rates, as well as at different vascular structures using the SMN.
Comparison of Human Hearts Preserved for 12 Hours in a Machine Perfusion Device versus Static Storage

Michael Cobert - UTSW

Introduction: An increasing number of patients on transplant waiting lists, and a shortage of available donors have amplified the need for new strategies in donor heart transplantation. In order to provide more options for surgeons a new technology has emerged that can shift the paradigm of donor heart placement, known as machine perfusion preservation. This technology has only been approved for clinical use in kidney transplantation, but results show improved organ function and recovery. Machine perfusion has the capability to increase the donor pool by extending the ischemic interval and procurement of marginal donor hearts. We have previously demonstrated that antegrade machine perfusion is metabolically superior to static preservation, but can cause aortic valve competence and non-nutrient flow. Another machine perfusion method being investigated by our laboratory is retrograde perfusion through the coronary sinus. This technique is used in cardiac surgery, but its application for machine perfusion has not been thoroughly evaluated. This study tests the hypothesis that retrograde perfusion reliably supports myocardial metabolism over an extended donor ischemic interval.

Materials and Methods: Human hearts obtained from brain dead donors rejected for transplantation were preserved for 12 hours in University of Wisconsin Machine Perfusion Solution by one of three techniques: 1. Static hypothermic storage (n=10) 2. Antegrade perfusion (AP, n=9) or 3. Retrograde perfusion (RP, n=8). Hearts from groups 2 and 3 were perfused at 5°C with a pre-clinical heart machine perfusion device. Temperature, flow rate, and perfusion pressure were measured continuously in perfused hearts. After 12 hours, myocardial oxygen consumption (MVO₂) and lactate accumulation in the preservation solution were measured in all groups. Ventricular tissue was collected, from each trial, for proton magnetic resonance spectroscopy (MRS) to evaluate the metabolic state of the myocardium. Colored microspheres were used to assess regional capillary flow in some perfused hearts. Myocardial water content was measured at end-experiment.

Results and Discussion: Stable temperature, pressure, and vascular resistance were maintained throughout the 12 hour perfusion period with both perfusion techniques. Lactate/alanine ratios were lowest in RP hearts, 0.5±0.3, and significantly higher in static hearts, 4.7±0.8 (p<0.05). AP hearts had a lactate/alanine ratio of 1.2±0.4. A trend towards greater myocardial water content was observed in RP hearts, although the difference did not reach significance, see Table. In the RP group, microsphere analysis suggested reduced RV nutrient flow, but overall preserved myocyte metabolism as assessed by MVO₂ and MRS data. Lactate accumulation (AP 2.0±0.7, RP 1.7±0.1 mM) and MVO₂ (AP 10.6±2, RP 9.1±1 mL O₂/100g/min) were similar amongst machine perfusion groups (p=NS).

Conclusions: Machine perfusion by either AP or RP technique can support myocardial metabolism of human hearts over extended intervals. RP may be superior to AP for maintaining metrics of myocardial oxidative metabolism, lactate/alanine ratio, but may increase myocardial edema, as indicated by myocardial water content. Machine perfusion appears to be a more viable option, compared to static storage, for long term preservation of human donor hearts.

<table>
<thead>
<tr>
<th>Group</th>
<th>Lactate/Alanine</th>
<th>Water Content (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Static</td>
<td>4.7±0.8*</td>
<td>77±2</td>
</tr>
<tr>
<td>Antegrade</td>
<td>1.2±0.4</td>
<td>77±1</td>
</tr>
<tr>
<td>Retrograde</td>
<td>0.5±0.3</td>
<td>80±1</td>
</tr>
</tbody>
</table>

Data are Mean ± SEM. * - p<0.05 vs all other groups by ANOVA
A study of on-chip aqueous two phase system (ATPS) formation and its effectiveness in separation process

Pavithra Wijethunga - UTA

Aqueous two phase systems (ATPS) are generated by mixing aqueous solutions of two structurally different polymers (or one polymer and one salt) at high concentrations. These systems provides an attractive way to recover biological materials due to its gentle environment containing high water percentage and the low interfacial tension between phases that allows easy mass transfer. Although there are several reports that demonstrated biological sample separations on miniaturized devices using ATPS, none of them investigated the generation of ATPS on confined environment of microscale fluidic devices and its characteristics. Performing biological separations while ATPS is forming may help overcome the limitation of poor interaction between samples and reagents in confined environments. However, while ATPS formation in macro scale is supported by vigorous mixing and gravitational force, both mixing capability and gravitational force are insignificant in micro scale. Hence, in this study, we investigated the formation of ATPS on micro scale chip operated with an electrowetting on a dielectric (EWOD) principle. Droplets in nL volume of reagents were mixed and ATPS was successfully formed on EWOD chip. Furthermore, it was possible to separate the two phases into two droplets, demonstrating the potential capability of an effective on-chip biological samples (e.g. cells and macro biomolecules) separation while ATPS formation. This study aims to enhance the on-chip liquid-liquid extraction by using ATPS and to develop the concept of on-chip digital chromatography. Also we compare the characteristics of ATPS generated on-chip with that of the ATPS generated in macro scale and recognize how the difference can be explained using diffusion and convective mixing theories. This study further investigates whether the achieving right ATPS configuration in microfluidic environment depends on any factors such as the final phase volume ratio of the ATPS.
Characterization of ECG Signal using Programmable System on Chip (PSoC)

Anusha Ravuru – University of North Texas

Introduction

Electrocardiography (ECG) monitor is a medical device for recording the electrical activities of the heart using electrodes placed on the body. Personal ECG monitoring system is portable and easy to use. They reduce the number of hospital visits and are cost-effective solutions to rising health care costs. The main goal of this research is characterizing the ECG signal.

Aim and Method

There are many ECG monitors in the market but it is essential to find the accuracy with which they generate results. Accuracy depends on the processing of the ECG signal which contains several noises and the algorithms used for detecting peaks. Based on these peaks the abnormality in the functioning of the heart can be found. Hence we characterized the ECG signal which helps to detect the abnormalities and determine the accuracy of the system.

Results and Conclusion

We designed a portable ECG system using Programmable System on Chip (PSoC) device which processes and analyzes the ECG signal. Here we are using PSoC creator for hardware and software programming, to process the ECG signal and to detect peaks. The contaminated ECG signal is passed through various amplifies and filters to remove different kinds of noises. This processed signal is converted to digital signal and notch filtering is done through software programming. For the obtained signal P, Q, R, S, T peaks and their duration is detected through a C code. This information about ECG signal and peaks can be communicated to physicians in different ways as PSoC has several dominant modules. Here we used UART communication to communicate to PC through RS232. From PC the information can be communicated to a physician in real time. Processed ECG signal and peaks are plotted using MATLAB to analyze and characterize the ECG signal. Hence with this analysis the accuracy of the system and peak detection algorithm can be determined.
LONG-GAP NERVE RECONSTRUCTION USING DECELLULARIZED NERVE GRAFTS FOR THE TREATMENT OF PERIPHERAL NERVE INJURIES

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ABSTRACT

Long-gap peripheral nerve injuries arising from tumor, trauma or birth-related injuries requiring nerve reconstruction are currently treated using nerve autografts and nerve allografts. Autografts are associated with limited supply and donor site morbidity. Allografts require transient immunosuppression with substantial associated risks. To overcome these limitations, we investigated the use of detergent-free decellularized nerve grafts to reconstruct long-gap nerve defects in a rodent model. We also compared the effects of exogenous cells seeded within the decellularized nerve grafts to study their contribution to nerve regeneration in this setting.

Nerve grafts were harvested from the sciatic nerves of 36 donor rats (300-350 g, male Lewis). Ninety recipient rats (250-300 g, male Lewis) were divided into five groups (6 animals per time point per group): (1) Nerve graft (NG, positive control), (2) Silicone tube (ST, negative control), (3) Decellularized nerve graft (DE), (4) Decellularized nerve graft seeded with Schwann cells (DE-SC), (5) Decellularized nerve graft seeded with skin-derived progenitor cells (DE-SKPs). Each recipient rat had a 3.5 cm graft sutured across a sciatic nerve transection injury, thus reconstructing a 3.5 cm long-gap nerve defect. Six animals from each group were harvested at 6 weeks, 8 weeks and 12 weeks after implantation. Nerve regeneration among groups was compared using semi-automated quantitative histomorphometry, gastrocnemius muscle tetanic force and gastrocnemius muscle moist weight.

Histomorphometry results indicated maximum growth in NG when compared to other groups, and DE and DE-SC showed comparable growth at 12 weeks. ST and DE-SKPs groups showed no regeneration up to 12 weeks. Muscle force data indicated maximum functional recovery in NG group, followed by DE and DE-SC. Muscle weight was fully consistent with these trends. In conclusion detergent-free, decellularized nerve grafts are sufficient to promote regeneration across long-gap peripheral nerve defects as an alternative to existing strategies.