Thesis No.: 107 Design of a novel non-contact temperature controlled surgical laser system

Name: Özgür Kaya, Year: 2023

Advisor(s): Murat Gülsoy/Fatma İnci Çilesiz

Abstract: Achieving repeatable and successful results without causing excessive collateral damage is of paramount importance for photothermal laser applications. Conventionally, dosimetry studies are conducted on laboratory animals to determine ideal laser parameters. Unfortunately, these predetermined parameters cannot ensure patient safety and treatment success in the clinic due to variance between optical and thermal characteristics among subjects. Controlling laser irradiation with tissue temperature feedback is the current gold standard for various photothermal treatments. In this dissertation, I present the development of a compact and easy to use non-contact radiometric temperature measurement and laser control system based on a commercial, inexpensive IRt/c sensor. This thesis study establishes the validity of my design that potentially makes temperature control more accessible in clinical environments. I have shown the ability of this system to maintain tissue temperature at a set value over extended durations (60 s) using ex vivo Wistar albino rat skin. Additionally, I evaluated the practical performance of this system by ex vivo photocoagulation of bovine liver using two independent variables: laser power and target temperature. Temperature-time responses of samples varied significantly, in agreement with our expectations, confirming a wide range of optical and thermal coefficients. Using target temperature as an independent variable, this system was successful in regulating the coagulation zone. Moreover, it was able to prevent undesired thermal damage in all but two samples (out of 144). I have also shown that this system can produce scientifically valuable information for photothermal characterization of tissues.

Thesis No.: 106 Design and Fabrication of Neural Culture Structures for Monitoring of Neural Implant Performance

Name: Bengü Aktaş, Year: 2023

Advisor(s): Bora Garipcan

Abstract: Enhancing neuroprosthetic biocompatibility requires refining approaches to reduce side effects from invasive devices. Physical, chemical, and bioactive design aspects of biomaterials are proven to be important for providing proper cell-to-cell, cell-tomaterial interactions. Modifying neural implant surfaces with bioactive cues, particularly employing cell adhesion molecules, shows promise in creating efficient interfaces. Within this concept, this study utilized N-Cadherin, NCAM and the mixture (1:1) of these molecules with the aim of modifying representative gold electrode surfaces to enhance neuron-electrode contact. The study assessed modifications on both undifferentiated and differentiated neuroblastoma SH-SY5Y cell lines. Successful modifications demonstrated biocompatibility with cell viability results, and notably, surfaces modified with NCAM and N-Cad/NCAM outperformed traditional poly-L-lysine (PLL) coatings in supporting neurite growth. The subsequent part of the study also included a comparison between NCAM-modified surfaces and Collagen type I coated surfaces which was used as the negative control, alongside conventional poly-D-lysine (PDL)/laminin coated surfaces. This investigation aimed to elucidate behavior in C8D1A astrocyte cells, provide insight into glial scar formation, and suggest potential strategies to attenuate cell responses. The results underscored the dual impact of NCAM molecules on astrocyte behavior and the intricate response induced by Collagen type I, contributing to an optimized approach for understanding cellular actions in the local environment and the development of alternative neural interfaces.

Keywords: Au Surface, N-Cad, NCAM, Cell Adhesion Molecules, SH-SY5Y Neuroblastoma Cells, C8D1A Astrocyte Type I Clone Cells, Collagen Type I.

Thesis No.: 105 sEMG-based ankle position and moment prediction in silico: Neural network approach and muscle selection

Name: Ahmet doğukan Keleş, Year: 2023

Advisor(s): Can Yücesoy

Abstract: Lower limb amputation is the partial or complete removal of a limb, and powered prostheses are the best solution for restoring amputees' locomotion abilities. Although recent advancements have enhanced their hardware, autonomous adaptation is required to achieve natural ambulation. The utilization of surface electromyogram (sEMG) holds promise, whereas real-time analysis is challenging. Also, a systematic analysis should be conducted for muscle selection to ensure compatibility with different levels of amputations. Therefore, the feature extraction was implemented for non-normalized sEMG amplitudes, and an economic algorithm minimizing sEMG input was sought. For the sake of different amputation level compatibility, a practical algorithm was aimed to limit the use of lower leg muscles. In this context, neural network-based algorithms with timing-based approaches utilizing sEMG amplitudes as inputs have been developed to (1) predict sagittal ankle position and moment during ground-level walking and (2) rank all muscle combinations based on success. Eight leg muscles were studied: tibialis anterior (TA), soleus (SO), medial gastrocnemius (MG), peroneus longus (PL), rectus femoris (RF), vastus medialis (VM), biceps femoris (BF) and gluteus maximus (GMax). The results showed the best-performing muscle variation was MG+RF+VM whereas, PL and GMax+VM were distinguished as the economic and practical variations ($r_{position}>0.90$, $r_{moment}>0.97$), respectively. The analysis regarding the effect of window size selection for feature extraction on prediction accuracy revealed that a window size of 150 ms demonstrated the best performance for the proposed neural network architecture. The cross-validation results supported the repeatability of the structure and methodology.

Thesis No.: 104 Fabrication of carboxymethyl cellulose/gelatin/calcium phosphate cement/carbon nanomaterial scaffolds for bone regeneration

Name: İlayda Duru, Year: 2023

Advisor(s): Duygu Ege

Abstract: Compressive strength and inherent osteogenic capacity of calcium phosphate cements (CPCs) remain relatively limited. In this thesis, first, powder and liquid phase of CPCs were optimized. After this, nanodiamond (ND) and Fullerenol (Ful) were incorporated into carboxymethyl cellulose/gelatin (CMC/Gel) CPCs to enhance their ability to promote compressive strength and bone formation, respectively. It was found that ND did not contribute to the compressive strength of CPCs in unfunctionalized form; however, it was efficient to reduce the setting time of cements. Besides ND, the biocompatible Ful particles were introduced into CPCs at concentrations of 0.02, 0.04, and 0.1 wt/v%. The addition of Ful at the highest concentration to CMC/Gel cements leaded to a decrease in setting times, attributed to enhanced hydrogen bonding facilitated by the hydroxyl groups of Ful. In vitro studies focusing on reactive oxygen species (ROS) scavenging demonstrated the antioxidant activity when Ful was incorporated into CMC/Gel cements and the scavenging capacity of the cement was highest for 0.02 and 0.04 wt/v% Ful concentrations. Additionally, in vitro cytotoxicity studies revealed that cements with 0.02 and 0.04 wt/v% Ful protected cellular viability. Furthermore, treating MC3T3-E1 pre-osteoblast cells with low-dose Ful cements leaded to an increase in osteogenic differentiation. These findings strongly suggest a correlation between the osteogenic abilities of Ful-loaded cements and their antioxidant activity levels. Thus, this study highlights the promising potential of ND and Ful for enhancing the performance of CPCs in bone reconstruction procedures.

Thesis No.: 103 Development of a combined photodynamic and sonodynamic therapy for the treatment of bacterial infections

Name: Heba Alagha, Year: 2023

Advisor(s): Murat Gülsoy

Abstract: Antimicrobial resistance is one of the biggest threats to global health. Developing new treatment modalities that can eradicate pathogens without inducing drug resistant strains, is of great necessity. Photodynamic therapy (PDT) is such a promising modality that aims to destroy pathogens using light-activated drugs, but is limited by the light penetration depth in tissues. Its close relative, sonodynamic therapy (SDT), has the capability to overcome this limitation, due to the superior tissue penetration of low-intensity ultrasound compared to light, but the full potential of this therapy has not been realized yet. The aim of this PhD research was to develop an efficient antimicrobial therapy via the combination of PDT and SDT. For this purpose, IR780 iodide loaded mesoporous silica nanoparticles were synthesized, and their antimicrobial photodynamic and sonodynamic potentials against gram-positive Staphylococcus aureus and methicillin resistant Staphylococcus aureus, and gram-negative Pseudomonas aeruginosa and multi drug resistant Pseudomonas aeruginosa, were investigated. The antimicrobial photodynamic and sonodynamic potentials of free IR780 iodide were also investigated. The outcomes of the conducted studies demonstrated that both IR780 iodide and IR780 iodide loaded mesoporous silica nanoparticles can be utilized as photo/sono therapeutic agents, for the effective inactivation of drug resistance bacteria. However, IR780 iodide loaded mesoporous silica nanoparticles are more suitable for clinical application.

Thesis No.: 102 Development of Novel Device Technolşogies for Safer MRI Guided Biopsy Procedures

Name: Doğangün Uzun, Year: 2023

Advisor(s): Özgür Kocatürk

Abstract: Interventional magnetic resonance imaging (iMRI) is a potent method that combines the benefits of minimally invasive procedures and the exquisite imaging capabilities of MRI. Therefore, performing biopsy operations under the guidance of real-time MR imaging can increase success and safety of operations by promising precise, accurate, and safe MR-guided biopsy operations. Designing visible and safe interventional equipment continues to be a major challenge in this field as MRI develops into a more accessible and suitable imaging modality for interventional procedures. In this thesis study novel device technologies that could improve the success of MR-guided biopsy procedures are introduced and tested. First, a novel optical fiber force sensor was designed and implemented into a needle to provide feedback on the axial force applied to the needle tip during MR-guided biopsy operations. Accurate force mea surement, differentiation of different tissue types via stiffness detection capabilities, and the performance of the sensor under MRI were successfully tested through in vitro experiments. Next, a novel method for increasing the visibility of MR-compatible interventional devices was introduced by using alternating current (AC) controlled conductive ink printed tracking markers. An elaborate analysis was performed to obtain the highest tracking marker conspicuity using the AC-controlled markers and three commonly used MRI pulse sequences. A Custom 20-gauge needle prototype and an MR-compatible current supply circuit were designed. MR-visibility and safety of the prototypes were tested through in-vitro experiments according to the international medical device test standards. Finally, the performance of the needle prototype and the current supply circuit was tested in a post-mortem animal experiment.

Thesis No.: 101 Development of nano/micromotors for potential cancer diagnosis and therapy

Name: Sezin Eren Demirbüken, Year: 2023

Advisor(s): Bora Garipcan

Abstract: Recent developments in nano/micromotor based smart drug delivery and diagnosis systems have gained much attention due to their efficient capabilities and unique features. Smart drug delivery systems are preferred for reduced side effects, increased effectiveness, and controlled release in specific locations. Nano/micromotors enable motion control and propulsion, leading to reduced drug concentration, faster delivery, and enhanced penetration into inaccessible tissues. Hence, in the first part of the thesis, self-functionalized polymer poly(3-aminophenylboronic acid) (PAPBA) enriched nanomotors were developed by conjugating Paclitaxel (PTX) to PAPBA/platinum (Pt)-nickel (Ni)/ Pt according to demonstrate their efficacy in smart drug delivery with catalytic propulsion. Controlled drug delivery was achieved by inducing Near-Infrared irradiation (NIR) and altering the pH. Drug release and interaction of PAPBA-enriched nanomotors loaded with drugs were studied using MCF-7 breast cancer cells. In the second study of the thesis, two segmented, gold (Au), iron-nickel (Fe - Ni) as metallic micromotors were synthesized according to carry out controlled release of anti-cancer drug doxorubicin (DOX) to breast cancer cells and diagnosis of breast cancer with magnetic propulsion. Au segment surface of electrochemical fabricated micromotors were engineered to provide drug (DOX) loading and antibody (antiHER2) immobilization as capturing agent. Engineered Au segment surface made possible controlled drug release in acidic cancerous environment. Magnetic (Fe-Ni) segment ensured controlled drug delivery to MCF-7. Spheroids with nano/micromotor drug delivery systems offer valuable insights for optimizing their clinical use. These approaches highlight the potential of nano/micromotors as smart drug delivery methods over conventional systems.

Thesis No.: 100 Human Muscle Structure-Function Relation in vivo Using Magnetic Resonance Imaging Modalities

Name: Agah Karakuzu, Year: 2022

Advisor(s): Can Yücesoy

Abstract: Non-uniform muscle deformation has become a frequent finding in biomechanics research, using imaging modalities operating at different resolution levels from sarcomeres to fascicles. Mainly due to technical limitations, interpretations of these findings are detached from a theoretical foundation that considers the muscle with mechanical links to its surrounding. To enable this vital consideration, this thesis aims at developing and testing the validity of a multimodal MRI method that bridges the understanding between non-uniform mechanical deformations and their myofascial origins, in-vivo. 1) Supplemented with DTI tractography, registration-based fiber direction deformations and principal strains on NVTs characterized the myofascial loads in relation to the strain heterogeneity pattern in active muscle (proximally shortened (up to 22%), distally lengthened (up to 108%) fascicles). Inter-subject deviations from the general pattern were in agreement with subject specific anatomy. 2) A multiverse analysis was performed on the tuning parameters of the demons registration algorithm to assess the validity of strain distribution pattern against algorithmic choices. Results showed that the overall deformation pattern was immune to such perturbations, yet the strains amplitudes underwent significant changes. 3) To add orthogonal information to the myofascial origin assessment and validation of strain distributions, quantitative and velocimetry MRI were used. T1 mapping showed promising results in associating microstructural content with the strain distribution pattern. SR patterns from 2D VEPC showed weak similarities with registration-based principal strains, whereas those from compressed sensing 4D-PC showed much better agreement. Collectively, these studies show a way forward for the understanding of in-vivo muscle structure function relationship with implications for muscle physiology in health and disease.

Thesis No.: 99 Development of Software Tools for Improved 1H Magnetic Resonance Spectroscopic Imaging

Name: Sevim Cengiz, Year: 2022

Advisor(s): Esin Öztürk Işık

Abstract: Proton magnetic resonance spectroscopic imaging (1H-MRSI) provides a non-invasive, spatially resolved evaluation of brain metabolism. However, there are some limitations of 1H-MRSI preventing its wider use in the clinics, including the spectral quality issues, partial volume effect, chemical shift artifact, and low spatial resolution. Additionally, it is necessary to create metabolite maps for analyzing spectral data along with other MRI modalities. In the first part of this study, a MATLAB-based open-source data analysis software for three-dimensional 1H-MRSI, called Oryx-MRSI, which includes modules for visualization of raw 1H-MRSI data and LCModel outputs, chemical shift correction, tissue fraction calculation, metabolite map production, and registration onto standard MNI152 brain atlas while providing automatic spectral quality control, is presented. Oryx-MRSI implements region of interest analysis at brain parcellations defined on MNI152 brain atlas. All generated metabolite maps are stored in NIfTI format. Oryx- MRSI is publicly available at Oryx-MRSI link along with six example datasets. In the second part of this study, we investigated metabolic changes of mild cognitive impairment in Parkinson's disease (PD-MCI) using 1H-MRSI data analyzed with Oryx-MRSI. Sixteen healthy controls (HC), 26 cognitively normal Parkinson's disease (PD-CN) patients, and 34 PD-MCI patients were scanned in this prospective study. Neuropsychological tests were performed, and three-dimensional 1H-MRSI was obtained at 3T. Metabolic parameters and neuropsychological test scores were compared between PD-MCI, PD-CN, and HC. The correlations between neuropsychological test scores and metabolic intensities were also assessed. Supervised machine learning algorithms were applied to classify HC, PD-CN, and PD-MCI groups based on metabolite levels. PD-MCI had a lower corrected total N-acetylaspartate over total creatine ratio (tNAA/tCr) in the right precentral gyrus, corresponding to the sensorimotor network ($p = 0.01$), and a lower tNAA over myoinositol ratio (tNAA/mI) at a part of the default mode network, corresponding to the retrosplenial cortex ($p = 0.04$) than PD-CN. The HC and PD-MCI patients were classified with an accuracy of 86.4% (sensitivity = 72.7% and specificity = 81.8%) using bagged trees. 1H-MRSI revealed metabolic changes in the default mode, ventral attention/salience, and sensorimotor networks of PD-MCI patients, which could be summarized mainly as 'posterior cortical metabolic changes' related with cognitive dysfunction. In the last part of this thesis, low spatial resolution problem of 1H-MRSI was tackled. The application of super resolution convolutional neural networks (SRCNN) and Enhanced Deep Residual Networks for Single Image Super-Resolution (EDSR) for increasing the spatial resolution of 1H-MRSI were investigated. Fluid attenuated inversion recovery (FLAIR), T1-weighted and T2-weighted magnetic resonance imaging (MRI) data and a fused MRI, which contained the three different structural MR images in each RGB channel, were used in training the SRCNN scheme. Additionally, T1- weighted MRIs were used for training the EDSR network. The spatial resolution of 1H-MRSI images were increased using both SRCNN and EDSR models trained

with the anatomical MR images. The results of the proposed technique were compared with bicubic interpolation in terms of peak signal to noise ratio. The spectral pattern of the super resolved images were similar to that of the original high resolution MRI. Our results indicated that deep learning based super resolution models would contribute to reconstructing higher resolution 1H-MRSI. This thesis contributed to the literature in terms of developing an open-source MRSI software called Oryx-MRSI, which provides an unprecedented detailed data anal- ysis pipeline for 1H-MRSI, identifying metabolic correlates of PD-MCI, which might aid the clinicians for the diagnosis of MCI, and implementing deep learning based super resolution approaches that might increase the spatial resolution of 1H-MRSI without a high cost of scan time.

Thesis No.: 98 Assessment of Active State Titin's Effects on Muscle Mechanics Using Finite Element Modeling

Name: Alican Onur Çankaya, Year: 2022

Advisor(s): Can Yücesoy

Abstract: Calcium dependent mechanical behaviors characterize titin's contribution to force production in three-myofilament paradigm: (1) Stiffening of PEVK (Proline, Glutamate, Valine, Lysine) segment, and (2) reduction of free-spring length via N2A-titin binding. This thesis is focused on the introduction of an alternative perspective to the analysis of titin with incorporating epimuscular myofascial loads. Isolated and integrated rat muscle finite element model variations were used with three titin models: passive state titin, active state titin-I and active state titin-II. Results of isolated model showed that active state titin-I and II limits sarcomere shortening (lm = 32.7mm: up to 10% and 20%, respectively). Such shorter sarcomere effect characterizes active state titin's mechanism of effects. Integrated models showed that the shorter sarcomere effect becomes an inconsistent and variable mechanism: Shorter sarcomere effect is further enhanced for proximal fascicle interfaces (by 30.2% and 31.0%, respectively) whereas it is also diminished for remaining fascicles (by 10.3% and 14.0%, respectively), but even a longer sarcomere effect is shown. Overall, titin's mechanism of effect and functionality are manipulated by epimuscular myofascial force transmission. This implies a new approach for the 3-miyofilament model: For the analysis of the components of the contractile machinery, contribution to force production and contribution to muscle mechanics should be assessed with alternative perspectives. Titin's calcium dependent mechanical behaviors belong to former as these increases its stiffness, whereas shorter sarcomere effect belongs to latter as this mechanism further translates its effect to other components as well as to length-force characteristics. These together comprehensively define titin's contribution as a third myofilament.

Thesis No.: 97 Investigation of Kinesio Taping Effect Mechanism with Novel Imaging Analyses

Name: Seda Yıldız, Year: 2022

Advisor(s): Can Yücesoy

Abstract: Kinesio Taping (KT) is an elastic therapeutic tape that is utilized for the prevention and treatment of various neuromusculoskeletal disorders and sports injuries. Despite its widespread use especially improving muscular function, there is a lack of understanding of its effects on muscular mechanics. In vivo analyzes of muscle mechanical response to external loads caused by KT is crucial to define its unknown action mechanism and to improve this kind of therapeutic approaches. Due to continuity of fascial system by muscular connective structures (epimysium, perimysium, and endomysium) and the interaction between muscle fibers and extra cellular matrix, loading effects imposed by KT are likely to be distributed to deep muscular fascia via force transmission. This thesis aims to address these effects by tensiomyography (TMG) and combination of Magnetic Resonance Imaging (MRI) based deformation and Diffusion Tensor Imaging (DTI) based fiber tracking analyzes. TMG analysis revealed that KT caused an increase in muscle tissue stiffness and a decrease in muscle rate of force development. Results of MRI-based deformation and DTI-based fiber tracking indicated that KT-imposed external loads lead to along-fascicle shear strains and along-fascicle length changes in terms of lengthening and shortening and strain distribution were heterogeneous for all subjects. In summary, non-invasive in vivo analyzes were used to evaluate the effects of KT on muscular mechanics. Among these analyzes, the TMG method was used to measure the effects of KT on the mechanical properties of the muscle, while the MRI and DTI methods were used to measure the effects of KT on along-muscle fascicle shear strains and length changes.

Thesis No.: 96 Skeletal Muscle Mechanics and Spasticity Management: Human and Animal Experiments

Name: Cemre Su Kaya Keleş, Year: 2022

Advisor(s): Can Yücesoy

Abstract: Being the most common motor disability in childhood, cerebral palsy (CP) describes a movement disorder for which the exact underlying mechanism is unclear, and no cure is available. Yet, local injection of botulinum toxin type-A (BTX-A) is used for spasticity management. In this thesis, the relationship between the mechanics of spastic muscles and the impaired joint motion was investigated in patients, and the long-term effects of BTX-A on muscular mechanics were assessed in animals. Experiments on spastic knee flexors showed that passive muscle forces are much less than active forces (e.g., 26%), and epimuscular myofascial force transmission (EMFT) arising from intermuscular mechanical interactions significantly increases active forces (up to 132%). Combined with musculoskeletal models developed based on gait analysis data, EMFT effects were shown to be compatible with metrics characterizing patients' pathological gait, indicating that intermuscular mechanical interactions may be a source of high flexor forces in flexed joint positions. Experiments in the rat anterior crural compartment showed that long-term after injection, BTX-A yields in addition to decreased active forces, both unintended (a narrower range of force exertion by 23% and increased passive forces by 12%, for the injected muscle) and uncontrolled effects (similar effects on compartmental muscles due to the spread of the toxin). BTX-A also leads to collagen content increase (by several folds) for muscles exposed, which explains elevated passive forces and impacts also active forces. These effects are of high potential clinical importance as they conflict with therapeutic goals. Particularly, controlling the effects of BTX-A on connective tissue adaptation is critical for better spasticity management.

Thesis No.: 95 Biomedical Applications of Sharkskin Mimicked Polymeric Membranes

Name: Sabra Rostami, Year: 2022

Advisor(s): Bora Garipcan

Abstract: Infection is one of the biggest challenges of implantable biomaterials. The difficulty of eliminating implant-associated infection imposes a huge burden on the patient's life quality aside from the considerable financial cost of the treatment. Thus, effective approaches must be explored to design biomaterials with enhanced antibacterial activity. Sharks have been investigated via biomimetic and bioinspiration approaches and discoveries have shown that sharkskin possesses antibacterial effects due to the reduced drag force on the skin whilst swimming which is because of their skin’s surface microstructure. In this thesis the antibacterial properties of sharkskin mimicked polymeric membranes in static conditions, with and without the aid of antibacterial and bactericidal chemicals was studied. The aim was to understand the adhesion behavior of both bacteria and mammalian cells onto the biomimicked polymeric membranes and how the surface topography affected these properties. Moreover, the impact of surface topography on drug release and bactericidal activity of these membranes was investigated by examining the physicochemical, antibacterial, and cytocompatibility properties of fabricated membranes. In vitro experiments were conducted to evaluate cellular responses of mammalian cells along with bactericidal properties using human keratinocyte (HaCaT), mouse fibroblast (L929), and human dermal primary fibroblast (HDFa) cell lines as model cells and Gram-negative Escherichia coli and Gram-positive Staphylococcus aureus bacterial strains as model bacteria species. The results presented in this thesis show that sharkskin polymeric membranes have great potential for reducing bacterial biofilm formation most probably via preventing bacterial adhesion. Also, the cell adhesion on these membranes can be enhanced via chemical modifications.

Thesis No.: 94 Indocyanine Green Loaded Poly(lactic acid) Nanoparticles Mediated Phototherapy of Cancer

Name: Melike Güney Akkurt , Year: 2022

Advisor(s): Murat Gülsoy

Abstract: Phototherapy is a promising approach for cancer treatment which can be utilized alone or in combination with other treatment modalities. Among the available photosensitizers for phototherapy, indocyanine green (ICG) merits special attention, owing to its near infrared absorption characteristics and low dark toxicity. However, a strong tendency for protein-binding and aggregate-forming limits its use as a phototherapeutic agent. Such a drawback can be eliminated with the utilization of nanosized drug delivery systems to encapsulate and protect ICG molecules. Numerous drug delivery systems incorporating ICG for phototherapeutic or imaging purposes are reported in the literature. However; these systems mostly contain other therapeutic agents as well, making it difficult to assess the effects of ICG alone. Hence, this study was aimed to explore the impact of only-ICG encapsulating polymeric nanoparticles as a phototherapeutic agent. Poly(lactic acid) nanoparticles produced via a single-step nanoprecipitation method for encapsulation and delivery of ICG molecules were used to this end and their phototherapeutic effects on prostate cancer cells were examined. This study demonstrated that ICG-encapsulating poly(lactic acid) nanoparticles could be utilized as a phototherapeutic agent in order to inhibit cellular viability on prostate cancer cells and that the decrease in cell viability was primarily due to photothermal effect.

Thesis No.: 93 Photodynamic therapy with upconversion nanoparticles

Name: Burcu Güleryüz, Year: 2022

Advisor(s): Murat Gülsoy

Abstract: Photodynamic therapy (PDT) is an alternative approach to conventional methods (i e. chemotherapy and radiotherapy) that can be utilized to treat various cancers with less side effects. However, PDT has some restrictions such as photosensitizers delivery and light penetration depth. It was realized that these problems can be overcome with the improvements in nanotechnology; and today, many researchers have been initiated to study on PDT with various combinations of photosensitizers-nanoparticles. Recently, upconversion nanoparticles (UCNP) have revealed promising results with different surface designs. UCNP's unique anti-Stokes conversion capabilities enable the transmission of near-infrared (NIR) to visible light, providing a solution to the light penetration depth problem of traditional PDT. Since they have organic structure, UCNP do not show high biotoxicity and additional surface modifications allow photosensitizers delivery to the desired region of a body. In this study, Yb/Er doped UCNP was synthesized and coated with porous silica to merge MC540 and ZnPc photosensitizers. In order to prevent photosensitizers leakage over time and optically strengthen the nanoparticles for PDT activity, silica surface was conjugated with APTES-gold nanoparticles. Experiments on prostate cancer cells with this novel design revealed two notable results: (I) nanoplatforms exerted high biocompatibility that even 2 mg/ml concentration could be employed, and (II) the viability of cells was successfully reduced up to 35%. Furthermore, PDT effect of 3-4 nm sized gold nanoparticles on cells was detected for the first time.

Thesis No.: 92 Prediction of psychophysical responses from spike recordings in rat sensorimotor cortex by using Bayesian models

Name: Sevgi Öztürk, Year: 2021

Advisor(s): Burak Güçlü

Abstract: In this thesis, we studied the fundamental question in neuroscience: how perception is built based on the sensory stimuli from the physical world and turned into motor actions in the face of uncertain neural representations. The vast body of literature contains models using neural activity to decode stimulus parameters, motor responses, and behavioral patterns. In particular, this line of research became more important as sensorimotor neuroprostheses and brain-computer interfaces (BCI) were made possible by recent advances in technology. The real-time algorithms used in those applications have many limitations. The main goal of the thesis is to use Bayesian models to understand sensorimotor processing and develop a novel approach for future BCIs. Specifically, spike data were collected from awake behaving rats during psychophysical yes/no detection task. Within a Bayesian framework, task-related priors, posterior beliefs, and the objective function to match the observed choice of the animal were calculated. The random variables for stimulus presentation, population neural activity, and motor responses were combined in a probabilistic graph network. First, a somatosensory neuroprosthesis application is demonstrated. Next, the Bayesian model was used to predict trial-by-trial responses offline. It was found that psychophysically low-performing rats could be modelled better with the Bayesian approach. The simulation results were compared to predictions of other supervised learning algorithms (such as linear discriminant analysis, decision trees, etc.). The Bayesian prediction was one of best among those algorithms for low-performing rats. Finally, behavioral responses from previous trials and neural activity from the current trial were included in various Bayesian models, which studied the effects of incremental information to predict the behavioral response in the current trial. The results showed that the average firing rates in a population of neurons are mostly adequate to predict lever presses in the psychophysical task with high sensitivity and low bias. This thesis provides new insights into computational modeling to understand sensorimotor processing and development of future BCIs. Bayesian modeling can be particularly useful in rehabilitation and during the training period of neuroprostheses.

Thesis No.: 91 Bioimpedance spectroscopy in prediction of type I osteoporosis in menopaused women

Name: Fırat Matur, Year: 2021

Advisor(s): Özgür Kocatürk/Yekta Ülgen

Abstract: Bone mineral density (BMD) is a measure of survival for men and women, and it is used to diagnose Osteoporosis that can be diagnosed and treated with an effective screening. We measured bioimpedance spectroscopy (BIS) parameters of 129 menopaused women and compared them with their DEXA reference measurements. We observed a region specificity for the central BMD assessment using BIS. When sensing electrodes are on the dominant hand and infraclavicular fossa, dominant arm fc correlates with the hip BMD ($r = -0.412$; $P < 0.05$), and fcut for Osteoporosis is 49.565 kHz. When sensing electrodes are over the hands, fc correlates with lumbar BMD ($r = 0.580$; $P < 0.05$), and fcut is 32.4 kHz. BMI also affects BIS measurements, and if BMI < 30 kg/m2, the correlation of fc with the hip BMD is improved ($r = -0.456$; $P < 0.05$). fc may be alternatively calculated using the proposed original 3P-Nyquist method. Both fc and the phase angle of the impedance measured at a single frequency are a function of the same impedance model parameters, and measurement at a single frequency is less complicated than BIS. Phase angle of the measured impedance at 5 kHz has correlations with both lumbar ($r = 0.403$; $P < 0.05$) and hip ($r = 0.559$; $P < 0.05$) BMDs. When DEXA devices are not available or inaccessible, with its high mobility, non-invasive and cost-effective nature, BIS can be a good substitute in screening for BMD; however, clinical studies should be continued over a larger population to obtain the normative BIS cutoff frequency or phase angle values. A practical 2D-ROC method for combining two discrete markers in a 2-way classifier is also proposed: both for simulated and clinical data, the AV ERAGE function combining markers has higher correct classi cation rates than the individual markers.

Thesis No.: 90 Investigating The Brain Energy Dynamics During Language Activity

Name: Murat Can Mutlu, Year: 2021

Advisor(s): Hale Saybaşılı/ Reşit Canbeyli

Abstract: The present dissertation aimed to measure the overall cognitive cost of language and visual processing to the brain with ear temperature measurement. Three verbal auditory experiments revealed that processing words caused a greater temperature increase in the left ear than the right ear, indicating an expected left-hemispheric activity for language processing. Furthermore, processing words from a non-native language (English) caused greater cognitive cost (greater temperature increase) compared to words from the native language (Turkish). Lastly, it was found that the greatest temperature increase was caused by the most difficult task. The last auditory experiment assessed the frontal cortex hemodynamics with functional near-infrared spectroscopy (fNIRS) and showed that the left hemisphere was active throughout the experiment, while the most difficult task caused the most widespread neuronal activity. A visual discrimination task revealed a greater temperature increase in the right ear compared to the left ear. These findings suggested that ear temperature can capture the overall cognitive cost of lateralized brain functions and can dissociate the task difficulty. A novel mental rotation (MR) and Turkish relative clause (RC) processing experiments were carried out with fNIRS to further investigate the cognitive cost of visual and language processing as well as to assess the hemisphere's contributions to processing. The MR experiment revealed a core neuronal activity in the right hemisphere regardless of the task difficulty and increased left-hemispheric activity with increased task difficulty. RC processing in Turkish was investigated with a neuroimaging method for the first time and it was shown that processing object RCs causes greater cognitive load than subject RCs, reflected by more widespread neuronal activity in the prefrontal cortex and greater non-significant hemodynamic activity in Broca's Area.

Thesis No.: 89 Novel Biopsy Needle and Assisted Robotic System Design for Prostate Biopsy Procedure under MRI

Name: Davut İbrahim Mahçiçek, Year: 2021

Advisor(s): Özgür Kocatürk

Abstract: Prostate cancer (PCa) is one of the most common cancer type among men. The mortality rate for prostate cancer is signi cantly high compared to other common cancer types which makes it even more concerning for elderly males. For this reason the early and accurate diagnosis of PCa is vital to avoid deaths caused by PCa. In clinical practice, PCa is diagnosed with ultrasound guided biopsy procedure (TRUS-guided biopsy) after observing signs of PCa with di erent pre-screening methods. However, diagnosing PCa with the TRUS-guided prostate biopsy is controversial mainly because US imaging is not able to provide contrast di erence between healthy tissue and lesion. For this reason, biopsy samples are taken statistically from di erent regions of the prostate. On the other hand, magnetic resonance imaging (MRI) can help to distinguish lesions from healthy tissues. Therefore, the optimal way to perform prostate biopsy is to perform it under MRI guidance in order to eliminate accuracy concerns. In this thesis, a novel hydraulic needle delivery system that is designed for performing MRI-guided prostate biopsy procedure is proposed. The needle delivery system is composed of the main robotic unit, control unit, hydraulic actuator, biopsy gun and biopsy needle. All of these components were designed, manufactured and assembled in the scope of this thesis. The feasibility of the overall system was evaluated through in-vitro phantom experiments under an MRI guidance. The in vitro experiments performed using a certi ed prostate phantom (incorporating MRI visible lesions). MRI experiments showed that overall hydraulic biopsy needle delivery system has excellent MRI compatibility (SNR Loss < 3%), provides acceptable targeting accuracy (average 2.05 ± 0.46 mm) and procedure time (average 40 minutes).

Thesis No.: 88 Investigation of functional brain connectivity patterns in temporal lobe epilepsy

Name: Seda Nilgün Dumlu, Year: 2021

Advisor(s): Ahmet Ademoğlu

Abstract: In this study, functional connectivity using both Pearson and partial correlation coefficients and inter-subject variability were investigated in resting state functional resonance imaging (rs-fMRI) scans that belong to healthy and temporal lobe epileptic (TLE) patient populations. The main purpose of this thesis is to reveal the discrepancies between the healthy population and the patients with TLE in terms of functional connectivity revealing the temporal dependency among different brain regions. According to inter-subject variability results, TLE population exhibited higher inter-subject variability in frontoparietal control, default mode, dorsal/ventral attention, visual, limbic and somatomotor networks in line with the broad seizure onset and propagation pathway. We mostly found a significantly reduced functional connectivity in bilateral frontoparietal control, somatomotor, default mode and ventral attention networks with an implication of dysfunctioning in attention, long/short term memory, cognitive functioning and consciousness in patients with TLE as a result of 17-network parcellation. We also found a decreased functional connectivity between/within the networks of the frontoparietal control, the default mode and the ventral attention implying that these three networks as well show a variability, although to a lesser extent. This result signifies these networks are severely deteriorated in patients with TLE. On the other hand, to compute the direct functional connectivity among different brain regions, partial correlation coefficients estimation is used. In doing so, we took advantage of Random Matrix Theory to well approximate the partial correlations, by virtue of, the inverse covariance matrices. As a result, the bilateral homologous structures in dorsal/ventral attention, frontoparietal control and default mode networks were also decreased in patient population confirming our results using Pearson's corelation coefficients.

Thesis No.: 87 A study in cultured neuronal networks

Name: Fazlı Kemal Bayat, Year: 2021

Advisor(s): Albert Güveniş/ H. Özcan Gülçür

Abstract: In this study, two platforms, combining multi-electrode arrays and optogenetic methods, were developed to study living neural networks in vitro. Both platforms,which included stimulation of neural networks developed in culture and monitoring of their activities, were tested using primary neuronal cultures obtained from mice and their operability and usability were demonstrated. In the first platform, dorsal root ganglion cells were made to emit fluorescent light when calcium influx occurs by optogenetic technique. In this platform stimulation was provided electrically through multiple electrode arrays and experiments were performed under fluorescent microscopy. The evoked activity was monitored through calcium transitions and the analyzed results revealed the network connections. Next, the network connections determined by analysis were confirmed by immunostaining that showed connections physically. The results obtained illustrated that the dorsal root ganglion nerve cells could establish connections with each other to form networks. In the second platform, hippocampal cells were used and neurons were made excitable with light using the optogenetic approach. After that, the optical stimulation using a digital micro mirror device for excitation was performed locally and focused. Spontaneous and stimulated extracellular electrical activity was monitored and recorded with multiple electrode arrays. On this platform, bilateral and closed-loop electrophysiology applications were performed and multi-channel and experiment examples were presented. The results show that the new platform designed for extracellular electrophysiology applications, with the option of multi-channel, artifact-free and closed-loop experimentation, eliminates the deficiencies and problems of those proposed in the previous studies. In conclusion, in the presented study, it has been shown that multi-electrode arrays can be successfully integrated with optogenetic methods that have both activity monitoring and stimulation purposes.

Thesis No.: 86 Deep learning approaches for the localization of capsule endoscope

Name: Kutsev Bengisu Özyörük, Year: 2021

Advisor(s): Bora Garipcan/ Mehmet Turan

Abstract: Deep learning techniques hold promise to develop dense topography reconstruction and pose estimation methods for endoscopic videos. However, currently available datasets do not support effective quantitative benchmarking. In this thesis, we introduce a comprehensive endoscopic simultaneous localization and mapping (SLAM) dataset consisting of 3D point cloud data for six porcine organs, capsule and standard endoscopy recordings, synthetically generated data as well as clinically in use conventional endoscope recording of the phantom colon with computed tomography scan ground truth. To verify the applicability of this data for use with real clinical systems, we recorded a video sequence with a state-of-the-art colonoscope from a full representation silicon colon phantom. Additionally, we propound Endo-SfMLearner, an unsupervised monocular depth and pose estimation method that combines residual networks with a spatial attention module in order to dictate the network to focus on distinguishable and highly textured tissue regions. The proposed approach makes use of a brightness-aware photometric loss to improve the robustness under fast frame-to-frame illumination changes that are commonly seen in endoscopic videos. To exemplify the use-case of the EndoSLAM dataset, the performance of Endo-SfMLearner is extensively compared with the state-of-the-art: SC-SfMLearner, Monodepth2, and SfMLearner.

Thesis No.: 85 Clinical grade medical device technologies for interventional cardiovascular magnetic resonance imaging procedures

Name: Dursun Korel Yıldırım, Year: 2021

Advisor(s): Özgür Kocatürk

Abstract: Magnetic Resonance Imaging (MRI) is a promising candidate against X-ray fluoroscopy for the image-guidance of minimally invasive procedures thanks to its ionizing radiation-free, exquisite soft tissue contrast and ability of 3D real-time imaging in arbitrary planes. However, interventional MRI (iMRI) is hampered by the lack of clinical grade MRI-compatible interventional devices. In this thesis study, first, a lowprofile iMRI device fabrication method was introduced by modifying the conductive ink printing method which was previously introduced by our group. Next, three most fundamental iMRI device designs including a 20 G active iMRI needle, a 0.035" outer diameter metallic active iMRI guidewire and a 6 FR, MRI-safe, metallic braided catheter were successfully introduced to expand interventional cardiovascular MRI applications. Electromagnetic simulation tools were employed to optimize the device radio frequency (RF) antenna geometry for optimal device visibility, and to assess RF-safety of iMRI devices. Proposed iMRI device designs were prototyped using biocompatible materials. In-vitro mechanical, RF-induced heating and MRI visibility performance of the prototypes were tested per international medical device test standards. In-vivo mechanical and MRI visibility tests were performed in swine per local animal study regulations. Test results were compared to commercially available equivalents. RF-induced temperature rise of all three prototypes remained within clinically acceptable limits. Active iMRI needle and active iMRI guidewire prototypes were clearly visible during in-vitro and in-vivo tests. All prototypes demonstrated comparable mechanical performance with commercially available equivalents. Proposed iMRI device designs will meet the most urgent need in the iMRI field enabling a broad range of iMRI applications.

Thesis No.: 84 Improved multi inversion time arterial spin labeling MRI of the brain

Name: Dilek Betül Arslan, Year: 2021

Advisor(s): Esin Öztürk Işık

Abstract: Arterial spin labeling magnetic resonance imaging (ASL MRI) measures cere- bral blood flow (CBF) quantitively without using any contrast agent or radiation.The calculation of labelled blood arrival time to tissue and arterial vessels provides hemody- namic information, which may be useful in understanding neurodegenerative disorders. Separate pseudo-continuous ASL (pCASL) MR can be done at multiple inversion times (TI) to avoid inaccurate CBF estimation due to uncertainties in arrival times, which is time consuming and limits the number of averages. ASL MRI using Look-Locker (LL) readout and the time-encoded pCASL MRI (te-pCASL) using Hadamard matrix are two approaches for acquiring ASL data at multiple TIs. ASL-MRI with LL readout requires a complex model to accurately estimate CBF. On the other hand, te-pCASL MRI has a shine-through effect, which might cause errors in CBF estimation. In the first part of this thesis, the brain perfusion deficits in Parkinson's disease with mild cognitive impairment (PD-MCI) were investigated using ASL MRI with LL readout. PD-MCI patients displayed a posterior hypoperfusion pattern, which classified these patients with over 90% accuracy in comparison to healthy controls. Moreover, geneti- cally risky PD with microtubule-associated protein tau gene (MAPT) H1/H1 haplotype had visual hypoperfusion as compared with non-risky PD. In the second part of the thesis, the possible reasons of shine-through effect in te-pCASL MRI were assessed using simulations and in-vivo data. Based on the theoretical model, pCASL and te- pCASL MRI resulted in the same ASL signals. On the other hand, our experimental results showed that the use of selective background suppression inversion pulses could lead to the appearance of the shine-through effect. Keywords: Arterial spin labeling, Parkinson's disease, mild cognitive impairment, te-pCASL, Look-Locker readout, Parkinson's disease, shine-through effect. vi ÖZET BEYNİN GELİŞTİRİLMİŞ ÇOKLU TERS ÇEVİRME SÜRELİ ATARDAMAR FIRIL ETİKETLEME MRG'Sİ Atardamar fırıl etiketleme manyetik rezonans görüntüleme (ASL MRG), her- hangi bir kontrast maddesi veya radyasyon kullanmadan beyin kan akışını (SKA) nicel olarak ölçer. Dokuya ve arteriyel damarlara etiketlenmiş kan varış süresinin hesaplan- ması, nörodejeneratif bozuklukların anlaşılmasında faydalı olabilecek hemodinamik bil- giler sağlar. Bu nedenle, zaman alan ve ortalama sayısını sınırlayan varış sürelerindeki belirsizliklerden kaynaklanan hatalı SKA'yı önlemek için birkaç farklı görüntüleme za- manında ayrı pCASL yapılabilir. Birden çok ters TIlarda ASL veri toplamak için Look-Locker (LL) okumasının kullanımına dayanan ASL MR ve Hadamard matrisini kullanan zaman kodlu sözde sürekli ASL MRI (te-pCASL) iki yaklaşımdır.LL okumalı ASL-MRI, SKA'yı doğru bir şekilde hesaplamak için karmaşık bir model gerektirir. Öte yandan, te-pCASL MRI, SKA hesaplamasında hatalara neden olabilecek bir parlama etkisine sahiptir. Bu tezin ilk bölümünde, hafif bilişsel bbozukluğu olan Parkinson Hastalığında (PH) beyin perfüzyon eksiklikleri, LL okumalı ASL MRG kullanılarak araştırılmıştır. Hafif bilişsel bozukluğu olan PH'nin sağlıklı kontrole kıyasla %90'ın üzerinde doğrulukla posterior hipoperfüzyon göstermiştir. Ayrıca, mikrotübül ilişkili protein tau geni (MAPT) H1/H1 haplotipine sahip genetik olarak riskli PD, riskli ol- mayan PD'ye göre görsel hipoperfüzyona sahipti. Tezin ikinci bölümünde, te-pCASL MRG'de parlama etkisinin

olası nedenleri simülasyonlar ve in-vivo veriler kullanılarak değerlendirilmiştir. Teorik modele dayalı olarak, pCASL ve te-pCASL MRI, aynı ASL sinyalleriyle sonuçlandı. Öte yandan, deneysel sonuçlarımız, seçmeli arka plan bastırma çevirme darbelerinin kullanımının, parlama etkisinin ortaya çıkmasına yol açabileceğini gösterdi.

Thesis No.: 83 Development Of A Hybrid Methodology For Investıgatıon and Manıpulatıon Of Functıonal Mechanısmıs Of Bıologıcal Macromolecules With A Focus On Non-Globular Proteıns

Name: Burçin Acar, Year: 2021

Advisor(s): Prof.Dr.Ahmet Ademoğlu

Abstract: Anisotropic Network Model (ANM) guided Langevin Dynamics (LD) method (ANM-LD) is an enhanced sampling algorithm, in-house developed to study conformational changes between functional protein structures, that are not possible by traditional techniques. In this thesis, the applicability of ANM-LD was validated on various non-globular systems, then assessed on vitamin B12 importer BtuCD by means of experimental observations and comparison of computational outcomes with maltose importer MalFGK2 and lipid-linked oligosaccharide flippase PglK. ANM-LD succeeded to extract the mechanistic differences among these transporters while predicting fluctuations and allosteric couplings of BtuCD residues in agreement with previous experiments and observed FRET intensities. The dynamically key residues enabling the sampled transition were defined as functional residue networks and their estimated perturbation response were highly agreeable with the functional assays of the BtuCD mutants on these sites (25 out of 26 mutants functioned as predicted). Later ANM-LD algorithm was advanced to improve sampling, then tested on case systems c-Src kinase and BtuCD. In c-src kinase, these enhancements enabled to predict dynamically key sites that overlapped with known oncogenic mutation sites. In BtuCD, diversification of guiding modes resulted in alternative transition pathways. Consequently with its practicality and modularity; ANM-LD stands as an efficient tool to study protein dynamics and their working mechanisms and to extract allosteric communication networks, toward the aim of controlling protein function. Keywords: Computational Sampling Methods, Protein Dynamics, Enhanced Sampling Methods, ANM-LD, Conformational Change, Elastic Network Model.

Thesis No.: 82 Biomimetic polydimethylsiloxane cell substrate design for enhanced in vitro cellular behavior

Name: Meftune Özgen Öztürk Öncel, Year: 2021

Advisor(s): Prof.Dr. Bora Garipcan

Abstract: Recent developments in cell-based therapies and toxicological investigations reveal the need for well-designed, stable and flexible cell substrates. Mimicking the natural cellular microenvironment by altering cell substrate properties (stiffness, topography and chemical/biochemical composition) can significantly affect cell-substrate interfacial characteristics and potentially influence cellular behavior. Hence, the main objective of this thesis is to design biomimetic Polydimethylsiloxane (PDMS) cell substrates to enhance in vitro behavior of target cell types. In the first study, simple and one-step surface modification of PDMS is successfully accomplished by the preparation of amino acid (histidine, His; and leucine, Leu) conjugated self-assembled monolayers (SAMs) for enhanced osteoblast proliferation, morphology, alkaline phosphatase activity and mineralization. In the second study, PDMS substrates with healthy myocardium-like stiffness are produced and modified with conventional [(3-aminopropyl)triethoxysilane, APTES; octadecyltrimethoxysilane, OTS] and amino acid (His, Leu) conjugated SAMs. Comparative effects of these substrates are investigated on induced pluripotent stem cell (iPSC) behavior and their differentiation into cardiomyocytes. The last study is developed by using PDMS with a cornea-friendly stiffness, corneal endothelial cell (CEC) microenvironment-mimetic white rose petal topography patterning and collagen IV or hyaluronic acid modification for enhanced CEC proliferation, morphology and increased phenotypic marker expression. All these biomimetic approaches demonstrate successful platforms to improve cell substrate properties of PDMS, rendering very promising tools for cell-based therapies, microfluidics, drug screening and organ-on-chip platforms.

Keywords: Polydimethylsiloxane, Biomimetic, Self-assembled monolayer, Osteoblasts, Induced pluripotent stem cells, Cardiomyocyte differentiation, Corneal endothelial cells.

Thesis No.: 81 Biophysical approaches for modulating neural differentiation

Name: Alp Özgün, Year: 2021

Advisor(s): Prof.Dr. Bora Garipcan

Abstract: Neural differentiation of stem cells is central to regenerative strategies towards neurodegenerative diseases. The vast majority of literature shows chemical, biochemical and genetic approaches to control and utilize intrinsic or extrinsic stem cells for neural regeneration. However, biophysical factors are also able to regulate stem cell fate with some added advantages. They can be administered to organisms completely non-invasively or used as an integral part of in vitro models. Effects of substrate stiffness and electromagnetic fields on neural differentiation are reported in the literature but common for both is a lack of understanding how these biophysical factors interact with cells. The overarching goal of this thesis is to reveal new clues about the effect mechanism of these factors on neural differentiation. Towards this end, three different in vitro neural differentiation models were used in a mechanistic investigation. In the first segment, the results highlight a novel, integrin-independent and biomimetic mechanosensitivity of human neuroblastoma differentiation, along with new caveats attached to using this in vitro biological model. The following segments on electromagnetic fields reveal an unprecedented finding where zinc ions rush into the cells during chronic exposure to 50 Hz electromagnetic field and facilitate other, previously known effects of electromagnetic fields. Moreover, two different ion channels were associated with these effects, for the first time in the literature. Overall, the output of this thesis identifies three new key players for sensing biophysical factors during neural differentiation that will subtantially contribute to future efforts towards their utilization in neural regeneration research.

Keywords: Mechanotransduction, extremely low frequency electromagnetic fields, neural differentiation, calcium influx, NMDA receptor, zinc, TRP channels

Thesis No.: 80 Customizable TDI-Based Whole Body X-Ray Scanner

Name: Fevzi Aytaç Durmaz, Year: 2020

Advisor(s): Cengizhan Öztürk

Abstract: Medical X-ray systems are the gold standard in certain cases of medical diagnostics for over 100 years. The main scope of our studies is to develop a new full-body X-ray scanner device using line scanner detectors, and a plug and integrate hardware controlled system, this new device called SyncBox. Main focus of this particular dissertation is to control the total electronics and mechatronic systems of the device. full body X-ray scanner will be useful for trauma studies and bone surveys, where its high image resolution will help to identify more detailed images. SyncBox control system is a novel patented idea, that helps to integrate X-ray device components more easily and securely. Syncbox will help researchers to build up new, customizable devices faster, and it could begin a new developmental and even an industrial standard for X-ray imaging.

Keywords: Medical Imaging, Open Source Hardware, Medical Device Development, X-ray Applications, X-ray Imaging Hardware

Thesis No.: 79 Development Of An Injectable Polymer-Calcium Phosphate Cement Composites For Bone Substitution

Name: Öznur Demir Oğuz, Year: 2020

Advisor(s): Duygu Ege

Abstract: Since the discovery of injectable calcium phosphate (CaP) cements, they are widely used to fill irregularly shaped bone defects. This created an alternative to more invasive methods such as use of autografts, allografts, xenografts and synthetic pre- shaped scaffolds. Hence, this thesis aimed to design an alternative injectable bone substitute (IBS) that can better accommodate CaP additives while preserving bone- like rheological properties and performance. In this thesis, an IBS was prepared by using methylcellulose (MC), gelatin and bioceramic powder mixture. Initially, three different powder to liquid (P/L) formulations were adjusted to investigate the chemical structure, rheological characteristics, handling, mechanical and in vitro degradation properties. Then, the effect of graphene oxide (GO) incorporation investigated by analyzing their physicochemical properties and in vitro responses. Results showed that the elastic modulus was increased up to 6.89 ± 2.25 MPa from 1.72 ± 0.76 MPa with the addition of 2 wt% GO on day 14. The extracted solution of the GO reinforced IBS was found to be biocompatible with bone marrow mesenchymal stem cells (BMMSCs). Finally, zoledronic acid (ZOL) was incorporated into IBS samples. Results showed that the presence of ZOL prolonged the setting time of the IBS samples. The mechanical properties decreased with ZOL addition and increased with the incorporation of GO which was found as 25.73 MPa. In in vitro cell studies, both the inhibitory effect of ZOL and GO loaded IBS on MCF-7 cells and proliferative effect on osteoblast cells were observed. In conclusion, the outcomes of this thesis indicated that prepared IBS may be promising candidates to fill bone defects and assist bone recovery for non-load bearing applications.

Thesis No.: 78 Development Of A Modular Software Platform For Digital X-Ray Systems

Name: Altay Brusan, Year: 2020

Advisor(s): Cengizhan Öztürk

Abstract: Health centers require full-body X-ray imaging in their busy trauma departments. Full-body X-ray scans are required for bone examinations such as diagnosis of osteoarthritis and degenerative changes in the lumbar spine. The most preferred solution is to take digital X-ray images and then to stitch them together via a dedicated software. This approach has limitations concerning imaging time, costs, applied dose, and image quality. An alternate solution that optimizes all these factors for full-body imaging is possible. This device employs Time Delay Integration (TDI) X-ray detector, a new digital X-ray sensor design, with higher resolution and sensitivity in comparison to conventional flat-panel detectors. This thesis introduces a software platform to build customizable X-ray scanners and its first implementation in a device with TDI detector. The software solution for TDI based full-body scanning involves novel ideas and approaches which improve the device performance in terms of the applied dose, quantitative image quality, and applicability in comparison to current available solutions. Although the software solution is implemented first for specific TDI scanner, the mentality behind the platform is to provide a solution for all kinds of X-ray machines. The software platform is a uni ed extensible architecture for any kind of X-ray machine.

Thesis No.: 77 Characterization Of AU, AU/GO And AU/RGO Surfaces For Cartoid Endothelial Cell Proliferation By Electrical Impedance Spectroscopy Method

Name: Fatma Gülden Şimşek Temiz, Year: 2020

Advisor(s): Bora Garipcan/ Yekta Ülgen

Abstract: Endothelium dysfunction may be the cause of cardiovascular diseases such as heart attack, aneurysm, or atherosclerosis. Thus understanding endothelial cell prop- erties helps explaining the reasons and treatment of cardiovascular diseases. Electrical impedance spectroscopy (EIS) is a real-time tool for evaluation of cell behavior. In this dissertation, human carotid artery endothelial cell (HCtAEC) proliferation on graphene derivatives was analyzed through EIS, optical images, Alamar Blue cell viability test and cell staining. Gold (Au) layers were deposited on glass surfaces by using photo-lithographic technique and plasma enhanced chemical vapor deposition. Graphene oxide (GO) was immobilized on Au electrodes through self-assembly mono- layers (Au/GO). Hydrazine vapor reduction process was performed in order to obtain reduced graphene oxide (rGO) surfaces (Au/rGO). Au, Au/GO and Au/rGO surfaces were examined through SEM images and water contact angle measurements. These coatings were performed on the electrodes used in EIS analysis. EIS analysis (100 Hz-1 MHz) was performed for HCtAECs cultured on the Au, Au/GO Au/rGO electrodes for 10 days. Results showed that GO and rGO coatings did not prevent neither the electrical measurements nor the cell proliferation. rGO had a positive effect on HCtAEC proliferation. The rate of increase of impedance change from Day 1 to Day 10 was nearly five-fold for all electrode surfaces. Alamar Blue assay performed to monitor cell proliferation rates between groups, and rGO has shown the highest Alamar Blue reduction value of 43.65 ± 8.79%. Acridine orange/propidium iodide (AO/PI) staining showed that cell viability on electrodes was similar to tissue culture plate.

Thesis No.: 76 A Macro-Structural Chracteristic Of Brain White Matter: "Dispersion" With Its Clinical And Technical Applications

Name: Ali Demir , Year: 2020

Advisor(s): Mehmed Özkan

Abstract: The main goal of this thesis is to find distinct macro-structural characteristics of brain white matter in the case of psychosis, where development of diagnostic imaging measures is necessary for early diagnosis and prospective studies. Given a tractogram data, which is a dense set of white matter fiber pathways of the whole brain obtained from diffusion magnetic resonance imaging, we propose to compute a global measure of dispersion for a voxel from the end point statistics of a set of fibers, which indicates complexity of the white matter voxel not locally but at macro scales. The findings on phantom data demonstrate sensitivity of the proposed measure to the tuning parameters and show its range characteristics. The findings on the real data demonstrate that proposed macro-structural dispersion information is found to be significant for discrimination of the schizophrenia and the bipolar patients from the healthy controls, especially when the frontally associative bundles such as cingulum and inferior occipito-frontal fasciculus are considered. The macroscopic dispersion measure is as informative as the local diffusion measures for the detection of changes in the white matter regions due to the psychosis. Beside, as a technical application, the dispersion map is considered and experimented for segmentation of cingulum. The findings of the thesis provide that the proposed measure is a potential diagnostic imaging marker in the case of psychosis and we contribute to the field of diagnostic research by generating a novel dispersion map of the brain that could be used for other clinical and technical applications.

Thesis No.: 75 Psychophysical Evaluation Of A Sensory Feedback System For Prosthetic Hands

Name: İpek Karakuş, Year: 2020

Advisor(s): Burak Güçlü

Abstract: In this study, a vibrotactile sensory feedback system was designed and tested in accordance with the discrete event-driven sensory feedback control paradigm. Novel approaches were applied in terms of data processing and psychophysical characterization. As the first part, the sensing and signal processing system was designed. Therefore, a robotic hand was equipped with force and bend sensors by mimicking receptors in human hand. The sensor data was recorded during a cylindrical grasping task, and classified for object type and movement phase. Among three machine learning algorithms (k-Nearest Neighbour, Multinomial Logistic Regression and Support Vector Machines), highest classification accuracy was obtained with k-nearest neighbor classifier and the results were promising for the subsequent work. In the second part, the sensory feedback system was designed using two vibrotactile actuators and a user-specific calibration method was presented. The actuators were placed on the upper arms of 10 able-bodied participants. A psychophysical characterization procedure was applied to determine the stimulation amplitudes for each participant specifically. Then, same-different discrimination and pattern recognition experiments were conducted to evaluate the discrimination and closed-set identification of stimuli with varying parameters. Finally, discrete-event driven feedback experiments were run by mapping the parameters of the stimuli to the discrete events related to class labels representing object/movement type. According to the results, the psychophysical characterization procedure was reliable. On the other hand, the performance in the complex tasks was not affected by the psychophysical variations across participants. Experimental results showed that the system can be used to provide object-type and movement-type related information in daily use of prosthetic devices.

Thesis No.: 74 Models to Assess The Quality of Stored Erythrocyte Suspensions by Diffuse Reflectance Measurements

Name: Osman Melih Can, Year: 2020

Advisor(s): Yekta Ülgen/ Bora Garipcan

Abstract: Legislation in transfusion medicine define hemolysis level as the quality measure for erythrocyte suspensions (ES). Since the golden standard test for hemolysis is destructive and causing wastage of units, the hemolysis levels of ES are currently assessed with deceptive visual inspection method and the national blood banks periodically perform statistical quality analysis by measuring the hemolysis levels of only few units on their expiration dates. There are numerous studies revealing negative consequences of storage lesions on recipients. Therefore, a non-invasive biomedical diagnostic technique should be developed for the quality of each stored ES, before administering them to especially critically ill patients. Transparent thin plastic blood bags allow optical measurements. Diffuse reflectance spectroscopy (DRS) can be utilized for rapid and non-invasive evaluation of stored blood quality. The purpose of this study is to create models for predicting the hemolysis level or free hemoglobin (FHB) concentration of ES, with spectral parameters acquired from non-invasive diffuse reflectance measurements. After attempts with mixed model, a physically based exponential theory was used and a model was created with fresh ES having negligible FHB to observe the effect of hematological variables on the diffuse reflectance spectra. High levels of goodness of fits were observed ($R^2 \sim 0.93$). A semi-empirical equation, expressing the reflectance as a linear function of the reduced scattering coefficient of ES, was utilized. Its validity was confirmed with Monte Carlo simulations. Finally, FHB concentrations in ES were modelled as the linear function of the reflectance and other hematological variables. The highest correlation coefficient between predicted and actual FHB concentrations was 0.89. The error rate of the model in diagnosis was about 10%.

Thesis No.: 73 Identifying CT Image Radiomic Biomakers for Predicting Immunotherapy Response of Non-SmallCell Lung Cancer Patients

Name: İlke Tunalı, Year: 2020

Advisor(s): Albert Güveniş

Abstract: Checkpoint blockade immunotherapy (IO) provides improved long-term survival in a subset of advanced stage non-small cell lung cancer (NSCLC) patients. However, highly predictive biomarkers of IO response are an unmet clinical need. In this thesis, pre-treatment clinical covariates and quantitative image-based features (i.e., Radiomics) were utilized to identify parsimonious models that predict rapid disease progression (RDP) phenotypes and survival outcomes among NSCLC patients treated with IO. As part of the thesis, four studies were conducted. First, novel prognostic and predictive computed tomography (CT) radiomic features utilizing radial gradient and radial deviation maps were created. One feature, RD outside-border SD, was found to be associated with overall survival in two independent NSCLC cohorts. Second, clinical-radiomic models that predicted RDP phenotypes, including hyperprogressive disease (HPD), were created in the setting of NSCLC IO. Among 228 NSCLC patients, parsimonious clinical-radiomic models with modest to high ability (area under the curves: 0.812 and 0.843) to predict RDP were identified. In the third study, stable and reproducible peritumoral and intratumoral CT radiomic features of lung lesions were identified to reduce the chance of spurious findings. In the fourth and final study, pre-treatment clinical covariates and radiomics were utilized to identify a parsimonious risk-model based on survival outcomes among 332 NSCLC patients treated with IO. The most predictive radiomic feature (GLCM inverse difference) was found to be positively associated with CAIX expression, using a gene-expression and an immunohistochemistry dataset.

Thesis No.: 72 Targetting Tumor Metabolism to Improve Immunotherapy Responses

Name: Sultan Damgacı, Year: 2020

Advisor(s): Albert Güveniş

Abstract: The acidic microenvironment of solid tumors has suppressing effects on immune cells, accordingly immunotherapy responses. This thesis composed of two main studies as measuring tumor pH with non-invasive methods using MRI/MRSI and targeting tumor acidity to improve immunotherapy responses. Firstly, we developed two different MR imaging techniques to monitor tumor pH. We have shown that the difference in pHs before and after L-DOS47 treatments were statistically significantly different than control mice. To our knowledge this is the first study demonstrates the neutralization ability of proposed drug in in-vivo models. The second aim of this dissertation was to develop combinatorial approaches have potential to be used in the clinic for patient benefits. This includes neutralization oftumoracidityinordertoimproveimmunotherapyresponseswithL-DOS47currently in clinical trials and well tolerated. We have demonstrated in-vivo that L-DOS47 treatment is effective to promote survival when combined with anti-PD1. Overall, under the scope of this study we were able to develop two imaging techniques with MRI to monitor tumor pH and elaborated a combinatorial treatment model in order to boost immunotherapy responses. Isovue, L-DOS47 and anti-PD1 are already approved by FDA to be used in the clinic which makes this study remarkable for a new clinical trial design.

Thesis No.: 71 Application Of Newborn Jaundice Determination And Design Of A Noninvasive Bilirubinometer

Name: Yunus Karamavuş, Year: 2019

Advisor(s): Mehmed Özkan

Abstract: Newborn jaundice (hyperbilirubinemia), which is seen in 65% of healthy newborns, is usually a harmless condition and passes without any treatment. However, 5% of the jaundiced babies develop kernictures which may cause irreversible brain damage. Therefore, detection and follow-up of jaundiced babies are very important. The most common method for the evaluation and follow-up of neonatal jaundice is measuring the level of total serum bilirubin (TSB). Transcutaneous bilirubin (TcB) measurement, which is an alternative for jaundice detection and monitoring, is a safe, easy, painless, cost-effective and fast method as well as being noninvasive. The application of TcB measurement uses visible field reflection spectroscopy to determine the level of jaundice in newborns. The aim of this thesis is to design algorithms which can determine the level of jaundice by nonlinear approaches using diffuse reflection spectra obtained from a specially developed device. In order to achieve this, TcB and TSB measurements were taken from 314 infants and prediction algorithms were developed. The TcB values predicted by the designed algorithms were compared with the TSB values of the paired measurement. In addition, the performance of the designed algorithms was compared with the widely used JM-103 transcutaneous bilirubinometer. All designed algorithms can predict jaundice level with correlation values between 0.932 and 0.943. The results of the comparisons were found to be promising for the use of transcutaneous bilirubinometer devices.

Thesis No.: 70 The Effects Of Synaptic Modulation On The Vibrotactile Responses Of Somatosensory Cortical Neurons Studied By Microinjection MicroStimulation And A Computational Model

Name: Bige Vardar, Year: 2019

Advisor(s): Burak Güçlü

Abstract: In this thesis, we studied the effects of synaptic modulation on the vibrotactile responses of somatosensory cortical neurons by three different methods: microinjection, microstimulation and a computational model. First, we recorded single-unit spikes evoked by sinusoidal (duration: 500 ms; frequency: 5, 40, and 250 Hz; amplitude: 100 _m) stimulation of the glabrous skin. The changes in the responses were studied with microinjection of aCSF (sham), bicuculline, AMPA and NMDA near the isolated neurons in anesthetized rats. All drugs increased average firing rates only during vibrotactile stimulation, and increased entrainment as measured by the vector strength of spike phases. The results suggest that three inhibitory factors shape the spike responses of the neurons. In a different experiment, we electrically stimulated Basal forebrain (BF), the main source of cortical cholinergic inputs, of anesthetized rats while recording single-unit (n=87) spike activity in the SI cortex. The vibrotactile responses were measured with and without BF stimulation (0.5-ms bipolar pulses (50 _A) at 100 Hz for 0.5 s). BF activation had short-term and long-lasting significant effects on entrainment, but being effective only at 5-Hz mechanical stimulation. BF activation did not cause significant main effects (regardless of cell type and layer) on the firing rate measures. Long-lasting effects of cholinergic activation on entrainment are dependent on cell type and layer, probably due to the projection pattern from BF. Lastly, a preliminary computational model was generated mimicking the vibrotactile responses observed in the first experiment. By changing the model parameters, the effects of synaptic inputs can be simulated. Overall, this thesis may help to understand clinical conditions regarding excitation-inhibition balance and cholinergic modulation.

Thesis No.: 69 Optimizing The Accuracy of Tumor Segmentation in PET for Radiotherapy Planning Using Blind Deconvolution Method

Name: Alpaslan Koç, Year: 2019

Advisor(s): Albert Güveniş

Abstract: Tumor segmentation accuracy greatly affects the effectiveness of radiotherapy procedures. Maximizing the segmentation accuracy has high medical significance in order to deliver the highest radiation dose to the target volume while protecting the healthy tissues. This dissertation aims to present an optimized method to minimize errors in the automated segmentation of tumors in PET images. Blind deconvolution was implemented in a region of interest encompassing the tumor with an iteration number determined from Contrast-to-Noise Ratios. The images were resampled. Several automatic segmentation algorithms were tested on three datasets: phantom, simulated geometric lesions inserted in real images, and simulated clinical images with real heterogeneous tumors for which ground truth was known. The volumes of the tumors were 0.49-26.34 cc, 0.64-1.52 cc, and 40.38-203.84 cc respectively for the three datasets. The widely available software tools MATLAB, MIPAV, and ITK-SNAP were used. With the use of the active contour with classification technique, the mean errors were reduced from 95.85% to 3.37%, from 815.63% to 17.45%, and from 32.61% to 6.80% for all the lesions of the phantom dataset, the simulated dataset, and the large lesions of the clinical PET dataset respectively. The computational time was reduced by a factor of more than 10 by the use of region-of-interest-based deconvolution. Contrast-to-Noise Ratio and Region-of- Interest based deconvolution have the potential to improve delineation accuracy for different sizes of homogeneous and heterogeneous tumors. Improvement is very important for smaller tumors. The algorithm may provide reduced computational time with respect to full deconvolution and can be implemented using widely available software tools.

Thesis No.: 68 Assessment of Local Muscle Deformations Using Muşti-Modal Imaging and Finite Element Modelling

Name: Uluç Pamuk, Year: 2019

Advisor(s): Can Yücesoy

Abstract: In vivo assessment of muscle deformations, including influence of non-muscular tissues such as NVTs, aponeuroses, fasciæ or overlying skin, is key due to functional relevance of tissue connectivity within limb. In integral framework of anatomy, understanding deformations in muscle and non-muscular connectome, and mechanical interactions therein, is crucial. Muscle deformations caused by external loads, e.g., KT, are conceivable and crucial to quantify when exploring KT's unknown action mechanism. Continuity of muscle fibers and extra-cellular matrix (ECM) is also of relevance. Titin was so far considered as passive spring of sarcomere, a view now changing due to its altered properties in active state. Yet, muscle fiber–ECM interaction can further change titin's influence. This thesis aims to address these by MRI image registration, DTI and FEM. MRI analyses of KT showed principal tissue strains deviated from KT loading direction. By DTI tractography and MRI analyses combined, muscle fiber and shear strains upon passive knee extension were determined. Strains were non-uniform along fascicles, which lengthened (8.7%) and shortened (7.5%), overall. Passive muscle FEM indicated role of NVT connectivity in imposing myofascial loads that cause strain non-uniformities. FEM with active titin showed increased total stress, with little increase from cross-bridges and much from titin. Depending on titin formulation, strain non-uniformities varied, yet persisted. Active force increased or leveled beyond optimum length. Strains were shorter overall: a shorter sarcomere effect. In sum, new non-invasive in vivo DTI and MRI methods are used to assess muscle tissue deformations; FEM allowed proposing new views incorporating epimuscular interactions within limb, with implications for muscle pathophysiology.

Thesis No.: 67 Strategies To Increase Photodynamic Therapy Efficacy On Conventional And Complex In Vitro Cancer Models

Name: Mustafa Kemal Ruhi, Year: 2019

Advisor(s): Murat Gülsoy

Abstract: Cancer is one of the leading causes of death worldwide. Due to the side-effects and inefficacy of the conventional cancer treatment methods, alternative modalities are researched. One of the alternatives, Photodynamic Therapy (PDT), is a photochemical approach, which is based on the activation of a photosensitive chemical (photosensitizer) by a specific light source for creating reactive oxygen species that are toxic to cancer cells. A number of in vitro and in vivo studies, as well as clinical trials, are conducted every year for increasing the efficacy of PDT. Combining different photosensitizers or developing new nanoconjugations for better targeting are some of the strategies. Apart from monolayer cell cultures and in vivo animal models, another important tool for testing new cancer treatment strategies is an advanced in vitro model that mimics certain physiological factors in tumor microenvironment. These factors include cell-to-cell interactions, hypoxic environments and some mechanical stresses that may affect tumor progression. This PhD study proposes different strategies to increase photodynamic therapy efficacy and tests these new protocols on conventional and complex in vitro models. The outcomes of the studies not only show the success of the proposed strategies, but also reveals the importance of in vitro models for cancer research.

Thesis No.: 66 Thın Fılm Based Semı_Actıve Rf Marker Desıgn For Interventıonal Mrı Devıces

Name: Engin Baysoy, Year: 2018

Advisor(s): Özgür Kocatürk

Abstract: Compared to the other imaging modalities Magnetic Resonance Imaging (MRI) system has many advantages. There is a great demand to carry out interventional cardiovascular procedures under MRI scanner. However, the lack of visible markers and MRI compatible interventional instruments and devices, is the main problem for realizing clinical applications with MRI guidance. In order to provide widespread usage of MRI for endovascular operations, commercial catheters and guidewires must be manufactured by considering many performance criteria including visualization, miniaturization, _exibility and safety. In this thesis, clinical grade biocompatible polymers and metals were used to manufacture clinical grade MRI compatible RF markers. Proposed RF marker was deposited on a non_planar biocompatible catheter surface by physical vapor deposition (PVD) technique using cylindrical laser_cut shadow masks, which kept the overall device pro_le low. The presented fabrication approach is highly reproducible, and versatile, allowing variation of micro coils, capacitors, and conducting layer designs that are crucial for tuning the speci_c resonant frequency of a RF marker. In adddition to aforementioned work, an orientation independent simulation model was developed and validated to obtain a reliable method for evaluating the designed RF marker structures in a MRI environment. Finite Element Method (FEM) simulations were carried out for di_erent RF coil designs to make the computational analysis of their electrical and magnetic characteristics in COMSOL Multiphysics program.

Thesis No.: 65 Desıgn Of A Dynamıc Optıcal Property Monıtorıng System: Studyıng The Effect Of Temperature Change

Name: Ercan Kara, Year: 2018

Advisor(s): Murat Gülsoy

Abstract: In laser applications, it is necessary to know the tissue optical properties before the treatment and how they change during the treatment. The optical monitoring system with double-integrating-sphere having a special sample heating apparatus was designed to investigate the e_ect of temperature on optical properties. Temperature dependent optical property changes was investigated using lipid emulsion. It was found that the re_ectance value showed negative correlation with temperature and transmittance showed positive correlation. Also, it was observed that the reduced scattering coe_cient obtained using an inverse adding-doubling method showed a negative correlation with temperature, but there was no statistically signi_cant change in absorption coe_cient. The e_ect of such optical property changes on the light propagation was displayed by Monte Carlo simulation. As a result, optical properties can change with temperature and this change must be taken into account for safer laser applications.

Thesis No.: 64 Laser Sterılızatıon Technıque For Root Canal Treatment: Investıgatıng The Use Of Hulıum Fıber Laser

Name: Ayşe Sena Sarp Kabaş, Year: 2018

Advisor(s): Murat Gülsoy

Abstract: Conventional endodontic treatment uses a chemomechanical protocol to eliminate all infected debris and take the bacteria out from the root canal in order to prevent the development of persisting apical periodontal inflamation. The inadequate penetration depth of irrigants and anatomical irregularities of root canal negatively affect the success of the treatment. Laser assisted endodontic treatment is a new and effective adjunctive method in root canal to enhance the quality of the conventional treatment. The aim of this study is to evaluate a new wavelength, 1940-nm thulium fiber laser, in endodontic studies and finding optimum parameter ranges for an antibacterial efficiency while protecting the health of root canal and paradontal tissues. This thesis study consists of preliminary and main experiment parts. Initiatory experiments were done in order to learn and practice in oral microbiology and laboratory protocols. Main part of this study has preliminary analyses for determining the optimum irradiation parameters with regard to the temperature increase and identifying the effective laser power and irradiation time ranges for a sufficient antibacterial effect in vitro. With the parameters obtained from the pre-studies, optimum parameters range for 1940-nm Thulium Fiber Laser assisted endodontic therapy was considered within the safest conditions. After definining 1 W for the maximum safe laser power in root canal therapy, antibacterial efficiencies of four different laser powers were compared. After obtaining an sterilization up to log kill of 3, optimum laser power was examined in three different irradiation times: 15s, 30s, and 60s. The results of colony forming unit (CFU) values concluded that 1 W with application for 30 seconds for 1940-nm Thulium fiber laser was the optimal dose to perform the maximum antibacterial efficiency preserve the healthy condition.

Thesis No.: 63 Depth Assessment Of An Absorber In A Semı-Infınıte Edıum By Contınuous Wave Dıffuse Reflectance.

Name: E. Burteçin Aksel, Year: 2018

Advisor(s): Murat Gülsoy

Abstract: A method to locate an absorber embedded in a semi-infnite turbid medium by spatially-resolved continuous-wave di_use re_ectance measurements is introduced. The possible of use the method as a priori information in di_use optical imaging is discussed. The depth of the absorber is assessed by single wavelength spatially-resolved continuous-wave di_use re_ectance measurements by two detectors in a radial row. The ratio of perturbations introduced by the defect at two detectors is used to be matched with Ratio-vs.-Depth curve which are generated by approximate formulae of continuous wave di_use re_ectance. The error due to approximation and the error in depth assessment are studied for di_erent cases revealing favorable source-detector placements with respect to planar position of the defect. The e_ect of lateral displacement of the source with respect to defect is studied. A strategy to overcome errors introduced by erroneous prediction of background medium optical properties is suggested. Theoretical results indicate that the depth of the absorber can be obtained with 0.1 mm precision independent of its absorption coe_cient and its size for the values chosen in the study. The approach is tested experimentally, and it is observed that theoretical results _t with experimental data.

Thesis No.: 62 Identification of Arterial Input Function in Perfusion Imaging with MR Angiography-Supported Semi-Automatic Method

Name: Bora Büyüksaraç, Year: 2018

Advisor(s): Mehmed Özkan

Abstract: This thesis aims to improve arterial input function (AIF) selection in DSC-MRI by using the information gathered through magnetic resonance angiography (MRA) and cluster analysis of the concentration time curve (CTC) parameters. MRA was utilized with a dual-purpose, identifying arterial locations during the parametric evaluation of CTCs in DSC-MRI, and avoiding shape distortions in AIF. The knowledge of arterial locations is essential to the research, as it guided the cluster analysis carried out with the CTC parameters of voxels located within and around the middle cerebral artery (MCA). Additionally, it enabled us to identify the voxels that meet the AIF criteria and those with distorted CTCs. The literature has developed the following criteria for selecting AIF: high peak height (PH), small full-width-at-half-maximum, (FWHM), early time-to-peak (TTP), and early arrival time (AT). However, it has been found that high PH and small FWHM may indicate a shape distortion due to partial volume effect (PVE). PVE is a common problem in AIF identification, which emerges when a voxel contains both artery and brain tissue. To avoid PVE, we included in our cluster analysis a recently introduced parameter, the SS:AUC ratio, which indicates the ratio of the mean steady state (SS) value (post-bolus equilibrium) to the area under the curve (AUC) of the first passage of contrast agent. We calculated the SS:AUC of VOF and used it as a reference in selecting AIF. By using this reference value, we managed to detect the CTCs that were not distorted by PVE. If the SS:AUC of AIF was far from the reference value, CBF was either under- or over-estimated by a maximum of 41.1 ± 14.3% and 36.6 ± 19.2%, respectively.

Thesis No.: 61 Corneal Welding via Infrared Lasers: in vitro & in vivo Studies

Name: Rıfat Rasier, Year: 2017

Advisor(s): Murat Gülsoy

Abstract: Infrared lasers can be used to weld soft tissues. Water molecules and also protein molecules such as collagen absorb the infrared energy and a temperature gradient can be created at the application site. Objective of this PhD thesis is to investigate the potential of infrared lasers for welding tissue to contact lens and also for cornea welding in order to seal corneal cuts done during cataract surgery. One of the new application in the field is our study about amniotic membrane welded to contact lens by 1470-nm diode laser: a novel method for sutureless amniotic membrane transplantation. This study showed a new method for laser welding of a tissue to contact lens for ophthalmologic application. Corneal welding is rather a new application area in laser medicine, and few studies reported successful welding dose for different infrared wavelengths. Full thickness, oneplane 3.2 mm long clear corneal cuts were done using a pre-calibrated knife. Laser power and irradiation duration were the parameters used and histological indicators of photothermal effect were observed. In the field of corneal laser welding we made experiments which 809-nm, 908-nm, 1070-nm and 1980-nm laser used to weld clear corneal incisions. According to these in-vitro studies and their histologic results, another experiment was planned to compare 1070-nm and 1890-nm wavelengths which we found the best results in previous studies. In this thesis, in vitro cornea laser welding experiments were performed also with 1470-nm diode laser which have high water absorption. According to preliminary results; in-vivo rabbit study was planned with the best two energy parameters options of 1470-nm diod laser which we had with the in-vitro study. Full thickness, one-plane 3.2 mm long clear corneal cuts were done using a pre- calibrated knife under anesthesia. After irradiation, rabbit cornea’s were observed in postoperative first day, first week, second week and forth week. In this thesis it is possible to find a wide range of studies and their results about laser welding. In the light of the findings of these studies it may be predicted that laser welding applications will have much more place in all biomedical applications.

Thesis No.: 60 Improvement of ASL Based MR Angiography for Novel Applications

Name: Onur Özyurt, Year: 2017

Advisor(s): Cengizhan Öztürk

Abstract: In this study, a custom four dimensional arterial spin labeling angiography (4D ASL) sequence and a proof-of-concept software tool to integrate 4D ASL data to routine scanning were implemented. One of the aims of this study was to test whether the combined use of 4D ASL and contrast-enhanced MR angiography (4D CE-MRA) can work as a prospective alternative to digital subtraction angiography (DSA) for the delineation of the AVM nidus in stereotactic radiosurgery (SRS) planning. Our results indicate that high reproducibility and agreement with experts are achievable without using DSA. The combined use of high temporal resolution 4D ASL and high spatial resolution and vessel-to-background contrast 4D CE-MRA provided sufficient spatiotemporal angiographic information for the delineation of AVM niduses. Another application of 4D ASL is the testing of arterial input models which are used for blood fow quantification in ASL perfusion studies. The accuracy of quantified parameters (blood flow, arterial transit times etc.) is significantly effected by the model choice. For this purpose, we have derived analytical solutions of a more realistic model describing the time evolution of the labeled blood. The effects of varying arterial input parameters on the theoretical ASL signal have been investigated.

Thesis No.: 59 Photobiomodulation on Human Osteoblasts and Osteogenic Differentiation of Adipose-Derived Stem Cells

Name: Gamze Bölükbaşı Ateş, Year: 2017

Advisor(s): Murat Gülsoy/ Bora Garipcan

Abstract: The present in vitro comparative study evaluated parameters of osteogenesis under the influence of photobiomodulation (PBM). PBM uses light in the visible and near infrared spectrum to induce a non-thermal process and to activate endogenous chromophores, which may result in therapeutic outcomes. Although the cellular and molecular mechanisms involved in the PBM are still unclear, studies suggest that reactive oxygen species (ROS) produced in response to PBM, can induce activation of many biological pathways. Adipose-derived stem cells are promising for use in regenerative medicine and promoting their osteogenic differentiation would be used in improving bone tissue healing and regeneration. The effects of PBM at two different wavelengths with three different energy densities on human osteoblasts and osteogenic differentiation of adipose-derived stem cells were investigated in this present study. Another purpose of the study was to associate the possible biostimulative effect of light with photosensitizers (PSs), which are light activated molecules that cause ROS generation. The cells were incubated with Indocyanine Green (ICG) and Methylene Blue (MB) prior to laser irradiation. Assays measuring the cell viability, cell proliferation, alkaline phosphatase activity (ALP), mineralization, ROS generation and osteoblast specific gene expressions were performed. The results of the present study showed that combined light and PS treatment does not result in a synergistic enhancement of PBM on cell viability and proliferation, but detailed analysis revealed that mineralization and ALP activity were altered following only light or photosensitizer mediated light applications. Whether biostimulative or inhibitory effect occurs after PBM and PS-combined PBM depends upon light dose and wavelength. The potential applications of PBM may be numerous but adequate and reliable evidence is necessary to recommend PBM for clinical use.

Thesis No.: 58 Laser Brain Surgery With Near Infrared Lasers: Investigation of The Optimal Parameters By Real-Time Temperature Monitoring

Name: Burcu Tunç Çamlıbel, Year: 2016

Advisor(s): Murat Gülsoy

Abstract: The thermal damage of the surrounding tissue can be an unwanted result of continuous-wave laser irradiation. In order to propose an effective way alternative to conventional surgical techniques, photothermal damage must be taken under control by a detailed dose study. Real-time temperature monitoring can be also an effective way to get rid of these side effects. The aim of this study was to overcome the side effects of photothermal interactions with a better establishment of experiments for investigating the photothermal effects of lasers and to specify optimal laser parameters in order to propose lasers in clinical use. In the present study, ablation/vaporization capability of three different infrared lasers operating at 980-nm, 1070-nm and 1940-nm were investigated through comparative experiments. All studies were performed ex vivo followed by in vivo with real-time temperature monitoring and male Wistar rats were used as an animal model. Animals were sacrificed immediately after the stereotaxic surgery for histological examinations. Sections were stained with Cresyl Fast Violet in order to measure the thermally altered areas. The relation between laser parameters, temperature changes and ablation efficiency were determined. The correlations between rate of temperature change and ablation efficiency were calculated. In conclusion, this comparative study showed that the change in temperature in the tissue during laser irradiation, even though the laser source is different in terms of wavelength, can be a good indicator for the characteristics of lesion created by the laser.

Thesis No.: 57 Laser Biostimulation and Monitorization of Wound Healing by Means of Bioimpedance Measurements

Name: Hakan Solmaz, Year: 2016

Advisor(s): Yekta Ülgen/ Murat Gülsoy

Abstract: Wound healing is critically important for the quality of life. Substantial number of patients suffering from non-healing chronic wounds and having serious difficulties in their daily life are reported in wound healing studies. However the exact mechanism of healing is not fully understood yet. Scientists have been investigating modalities for stimulating the wound healing process. Laser photobiomodulation has become widespread supporting the idea of therapeutic effects of laser irradiation in biological tissues recently. Conventional methods for following the healing generally lack of objectiveness and repeatability. Thus, a new non-invasive, repeatable and cost effective method was needed. The aim of this study was to investigate the laser photobiomodulation on wound healing and monitor the healing process in-vivo by means of multi-frequency electrical bioimpedance measurements. Photobiomodulated in-vitro cell proliferation examinations were followed by in-vivo experiments on cutaneous skin wounds. Changes in the electrical properties of the wounds were examined with multi-frequency electrical impedance measurements on predetermined days of healing. Morphological, histological and mechanical examinations were used to find out the relationship between electrical properties of tissues and cellular events occurring during the healing process. Our findings showed the biostimulating effects of laser irradiation both in-vitro and in-vivo. The electrical impedance measurement results supported the idea of laser biostimulation on healing of cutaneous skin wounds. It is also shown that electrical bioimpedance measurements may be considered as a supporting non-invasive method for monitoring the healing process of skin wounds.

Thesis No.: 56 Detailed Analysis of Voxel Based Morphometry

Name: Özlem Özmen Okur, Year: 2016

Advisor(s): Cengizhan Öztürk

Abstract: Voxel Based Morphometry, VBM, is one of the most widely used brain morphometry methods which aims to reveal the structural differences between the brain MR images of different populations. It is a whole brain and fully automatic approach in which all the images are registered onto a common template and then segmented into grey matter, white matter and cerebrospinal fluid. After an optional modulation step (regaining the original volume which is shrinked or enlarged during the registration), smoothing takes place in order to make the data more normally distributed and to diminish the inexact nature of the nonlinear registration. Finally, voxel-wise statistical operations are performed between the groups of the images. As revealed in several studies, changes in these steps and changes in their parameters might influence the resulting statistics. Although some short guidelines exist for conducting the processing stages, this thesis tries to explain each main step and gathers the discussions in the literature to make the VBM users aware of some pitfalls and limitations of VBM; and also gives brief descriptions about the other brain morphometry methods to give a view for where VBM stands at. In this thesis, the effect of modulation and masking strategy at the statistical stage were studied and concluded that not using the modulation and using average-based masking for the statistical part increased the detection power of VBM. Additionally, within the scope of this thesis, three clinical applications of VBM are performed and presented: Comparisons of the brain images of mathematicians, SSPE patients, and solvent abusers vs healthy controls.

Thesis No.: 55 Design and Application of Compartmentalized Platforms for Neurobiological Research

Name: Aysel Fışgın, Year: 2016

Advisor(s): Cengizhan Öztürk

Abstract: Conventional culture systems remain inadequate for comprehensive understanding of injury and regeneration in peripheral neurons that extend axons over long distances and through varying extracellular microenvironments. Therefore, a highly tailorable in vitro system, that allows studying in different in vitro models that mimics axonal injury, regeneration and nerve transplants is required. This dissertation presents the development and application of novel compartmentalized in vitro cell culture platforms, where cell bodies are cultured on one side and axons are allowed to grow to the other side through microchannels that connect the two fluidically isolated compartments. First, regenerative effects of members of the glial cell-line derived nerve growth factor (GDNF) family of ligands (GFLs) were investigated in a microfluidic physical injury model and GDNF was most potent in promoting axon outgrowth after axotomy. Next, the first high throughput compartmentalized microfluidic platform (HTCMP) is developed, which is an innovative model for in vitro assays in drug screening, where distal axonal degeneration can be modeled by manipulating compartments independently. By means of HTCMP, Flucinolone Acetonide (FA) is identified as a neuroprotective compound in vitro and validated in vivo that it demonstrates axonal protection from PIPN as well as relieving neuropathic pain. Finally, compartmentalized microfluidic platforms that mimics the isolated in vivo environment, are used in an in vitro model of stem cell replacement therapy for nerve injuries, and it is demonstrated that that the axons of mESC (mouse embryonic stem cell) derived motor neurons are myelinated by mESC derived oligodendrocytes.

Thesis No.: 54 Articial Tactile Sensation by Microstimulation of the Hindpaaw Represantaion in the Primary Somatosensory Cortex of Behaving Rats

Name: İsmail Devecioğlu, Year: 2016

Advisor(s): Burak Güçlü

Abstract: In this thesis, rats were trained to detect the presence or absence of bursts of mechanical sinusoidal vibrations (duration: 0.5 s, zero-to-peak amplitude: 200 μm, frequency: 40 Hz) delivered to the volar surface of their hindpaws in a novel vibrotactile operant chamber. In psychophysical experiments, psychometric curves were obtained for three frequencies (40 Hz, 60 Hz and 80 Hz). Then, the rats were implanted with microelectrodes in the hindpaw representation of the primary somatosensory cortex and trained to detect trains of biphasic charge-balanced current pulses (pulse width: 600 μs, current intensity: 20-200 μA)(ICMS). They further tested in psychophysical experiments and psychometric curves were obtained for ICMS detection as in vibrotactile experiments. The psychometric data collected from vibrotactile and ICMS experiments were fitted with surface functions using the stimulus intensity and frequency. Psychometric correspondence functions (PCFs) were constructed based on the psychometric functions of five rats. The PCFs were used to estimate current intensities for a given tactile stimulus intensity and frequency. The PCFs were validated in an additional experiment at five frequencies (40 Hz, 50 Hz, 60 Hz, 70 Hz and 80 Hz). In this experiment, the rats performing vibrotactile detection task were presented with unrewarded trials containing either a vibrotactile or an ICMS stimulus. The vibrotactile and ICMS intensities were matched based on PCFs. Kolmogorov-Smirnov statistic showed that the vibrotactile and ICMS stimuli produced similar psychometric curves in validation experiments (all p values >0.05 for 5 frequencies and 5 rats). Therefore, the PCF based method seems to be feasible for modulating the current intensities and frequency of ICMS in a somatosensory neuroprosthetic application.

Thesis No.: 53 SOD1 A4V Mutation Increases Nav 1.3 Channel Excitability on Xenopus Laevis Oocyte

Name: Elif Kubat Öktem, Year: 2016

Advisor(s): Yekta Ülgen/ Ata Akın

Abstract: Amyotrophic lateral sclerosis (ALS) is a lethal, paralytic disease caused by degeneration of motor neurons in the spinal cord, brain stem and motor cortex. Mutations in the gene encoding copper/zinc superoxide dismutase (SOD1) are present in 20 % of familial ALS and 2 % of all ALS cases. The most common SOD1 gene mutation in North America is a missense mutation substituting valine for alanine (A4V). In this study, sodium channel currents in oocytes expressing either wild type or mutant (A4V) SOD1 protein were analyzed. In this study elicited on Xenopus Laevis oocyte, it is demonstrated that the A4V mutation confers a propensity to hyperexcitability on a voltage dependent sodium channel (Nav) mediated by heightened total Na+ conductance and a hyperpolarizing shift in the voltage dependence of Nav 1.3 activation. To estimate the impact of these channel effects on excitability in an intact neuron, these changes were simulated in the program NEURON; this shows that the changes induced by mutant SOD1 increase the spontaneous firing frequency of the simulated neuron. These findings are consistent with the view that excessive excitability of neurons is one component in the pathogenesis of this disease.

Thesis No.: 52 Design Of A Collimation For Breast-Specific Gamma Imaging and Assessment Of Nec Rate For A Pet Scanner Using Monte-Carlo Simulations And Response Surface Methodology

Name: Didar Talat, Year: 2016

Advisor(s): Albert Güveniş

Abstract: This thesis is composed of two studies that demonstrate the implementation of Monte Carlo (MC) simulations and response surface methodology (RSM) to specific problems in planar and tomographic nuclear medicine imaging. In the first study, the collimator of a planar small field-of-view continuous crystal breast specific gamma camera is optimized by maximizing the lesion contrast-to-noise ratio (CNR) with respect to hole diameter, septal thickness and hole length. This study demonstrated that the pairwise interaction effects of the collimator parameters play a key role in determining the set of optimal parameter. As a result of optimization, a considerable improvement of up to 73% in CNR with respect to the reference collimators is achieved. Moreover, the critical region for detectability shifted towards the direction of smaller lesion diameter and lower tumor-to-background ratio. Another conclusion of the study is that the optimizer adapts itself to the spatial resolution/sensitivity trade-off as the lesion depth changes. Based on these findings, we conclude that the advantages obtained with this approach may lead to an advancement in collimator design. Whereas, the second study is involved with the positron emission tomography (PET) camera performance based on the noise-equivalent-count rate (NECR). In this part, the effect of lower energy threshold (LET) and coincidence time window (CTW) on NECR is investigated over a range of activities. Our findings showed that both LET and CTW showed signi_cant linear and quadratic effects. Moreover, the evidence of presence of interaction among parameters makes this approach superior in comparison to conventional one-variable-at-a-time assessment techniques. Through an in-depth viii literature review, the proposed approach is also shown to be useful for a range of cameras for both human and animal use, as well as organ-specific and time-of-flightPET scanners.

Thesis No.: 51 Assessment Of Effects Of Botulinum Toxin On Muscle Mechanics

Name: Ahu Nur Türkoğlu, Year: 2016

Advisor(s): Can Ali Yücesoy

Abstract: Effects of widely used Botulinum toxin (BTX) treatment on muscular mechanics are highly important, but their mechanism and time course are not well understood. Present thesis is focused on mechanical mechanism of BTX treatment using finite element method and animal experiments. In an isolated muscle model partial paralyzation is shown to cause (i) the sarcomeres to attain higher lengths throughout the entire muscle (e.g., at short muscle length, the inactivated fascicles of middle half paralyzed muscle and the same parts within BTX-free muscle shortened by 29-27% and 32-29%, respectively), (ii) enhanced potential of active force production of the non-paralyzed muscle parts (up to 14.5% for BTX cases), and (iii) decreased muscle length range of force exertion. It is shown that intramuscular myofascial force transmission is central to these effects. Additionally, experimental results showed diminished epimuscular MFT and intramuscular collagen increase. Due to information on the loss of interactions between muscles and increased ECM stiffness due to increased collagen, temporal changes within the muscle during treatment is examined. Modeling of time course of the BTX treatment showed that sarcomeres attain even higher lengths with increased ECM stiffness and is reversed at longer muscle lengths. Consequently, force production capacity of activated sarcomeres gets further enhanced in the long-term and a narrower length range of force exertion (20.3%, 27.1% and 3.4%, acute, long-term and post BTX treatment, respectively) is a consistent finding. If such stiffness increase were shown to remain post-treatment, enhanced capacity would become permanent for the entire muscle. It is concluded that mechanical effects and morphological changes shown can affect muscular mechanics adversely if not managed accordingly.

Thesis No.: 50 Tensor Analysis of Neuroimaging Data

Name: Esin Karahan Senvardar, Year: 2015

Advisor(s): Ahmet Ademoğlu

Abstract: Acquisition of large amounts of data in neuroimaging research requires development of new methods that can disentangle the underlying information and reveal the features related to cognitive processes. This thesis attempts to propose new methods that favor the multimodality and multidimensionality of the brain data. The main difficulty for the fusion of imaging modalities is the discrepancies in their spatial and temporal resolutions as well as the different physiological processes they reflect. This problem is addressed by decomposing the EEG and fMRI data cast as tensors on both common and discriminant subspaces and computing the common spatial profile from the data on the cortical surface. The Granger causality analysis of brain connectivity is reformulated on tensor space enabling incorporation of tools developed in that area of research. The first approach on this analysis facilitated tensor methods for sparse representation of the connectivity patterns whereas the second method resolved them as atomic structures. General theory and computationally efficient algorithms are presented. The techniques are illustrated on the simultaneous EEG/fMRI recordings for the fusion model and on the fast fMRI data for the connectivity analysis. The proposed approaches may have a wide application area ranging from the early diagnosis of neurological diseases to the brain-computer interface studies.

Thesis No.: 49 Nonlinear State and Parameter Estimation of the Hemodynamic Model Using fMRI Bold Signal

Name: Serdar Aslan, Year: 2015

Advisor(s): Ahmet Ademoğlu/ Ata Akın

Abstract: The joint estimation of the parameters and the states of the hemodynamic model from the blood oxygen level dependent (BOLD) signal is a challenging problem. In the functional magnetic resonance imaging (fMRI) literature, quite interestingly, many proposed algorithms work only as a filtering method. In the fMRI state estimation literature, extended Kalman filter (EKF) is asserted to be not robust and worse than standard particle filters (PF). We compared EKF with PF and observed that the contrary is true. We also implemented particle filter that approximates the proposal function by the extended Kalman filter. We compared Gaussian type approximated estimation techniques like extended Kalman filter (EKF), unscented Kalman filter (UKF), cubature Kalman filter (CKF) as well as stochastic inference techniques like standard particle filters (PF) and auxiliary particle filter (APF). Filtering makes the estimation of the hidden states and the parameters less reliable compared with the algorithms that use smoothing. We improved the EKF performance by adding smoother. The joint state and parameter estimation is improved substantially by performing the iterative EKS (IEKS) algorithm. We compared IEKS performance with the square-root cubature Kalman smoother (SCKS) algorithm. We show that its accuracy for the state and the parameter estimation is better and much faster than iterative SCKS. SCKS was found to be a better estimator than the dynamic expectation maximization (DEM), EKF, local linearization _lter (LLF) and PF methods. We show in this thesis that IEKS is a better estimator than iterative SCKS under different process and measurement noise conditions.

Thesis No.: 48 A Hybrid Biological/ In Silico Neural Network Based Brain Machine Interface

Name: Mehmet Kocatürk, Year: 2015

Advisor(s): Albert Güveniş/ H. Özcan Gülçür

Abstract: Brain-machine interfaces (BMIs) aim to improve the lives of individuals with neurological disease or injury, by opening new information transfer channels between brain tissue and prosthetic actuators. In a majority of the BMI work, the data acquired from the motor cortex neurons are decoded into user's intended prosthetic actions by some "optimized" input-output mathematical model. Although this approach is quite sound, the information processing principles used are fundamentally different from those of natural neural circuits. In this thesis, we propose a novel, neurally-inspired design approach; the BMI controller consists of spiking model neurons and receives simulated synaptic inputs from extracellularly recorded neurons. The controller therefore forms a hybrid biological/in silico neural network with the neuronal circuits of the user's brain. In order to fulfill the challenging real-time requirements of the present design approach, we first developed the Bioinspired Model Development Environment (BMDE). The BMDE, implemented on a hard real-time system, significantly facilitates BMI model development processes with powerful online data visualization tools while satisfying the strict timing constraints of the proposed design approach. Using the BMDE, we realized a novel, adaptive BMI controller which consists of in silico striatal medium spiny neurons, each receiving simulated synaptic inputs from extracellularly recorded motor cortex neurons. By implementing a reward-modulated spike timing-dependent plasticity rule and a winner-takes-all mechanism, the BMI controller, based on real-time closed-loop simulations, achieves perfect target reach accuracy for a two target reaching task in one dimensional space. Using this design approach and the BMDE, new generation BMI controllers that better mimic brain circuits can be developed. Moreover, by investigating the interactions between biological and in silico neural networks during neuroprosthetic control tryouts new neuroscienti_c insights concerning motor control and learning can be obtained.

Thesis No.: 47 An Optoelectronic Systems for Device Localization in Interventional MRI

Name: Murat Tümer, Year: 2015

Advisor(s): Yekta Ülgen/ Cengizhan Öztürk

Abstract: In active catheter tracking, a microcoil directly connected to the MRI system and positioned at the distal end of the catheter is employed for localization. The peaks in the frequency spectrum of the acquired MR signal correspond to catheter's physical location. The major problem with active techniques is the RF heating due to long conducting wires. Fully optical systems that replace the conducting wires with inherently RF-safe optical fibers are proposed. In these systems, the SNR suffers from the electro-optical signal conversion distally (and opto-electrical conversion proximally) at this high frequency. Amplifying and frequency down-converting the MR signal at the catheter tip could minimize signal losses. Amplification could be achieved with an LNA placed next to the microcoil. To provide the reference signal to the mixer for frequency down-conversion of the amplified MR signal, an outside generator or on-chip oscillator could be used. Both methods have their disadvantages like increased complexity at the distal end due to additional cable and frequency drift over time due to temperature or bias voltage variations. In this work, the reference signal for frequency down-conversion is provided from the MRI scanner's own transmitter! It is a very reliable source of signal since no frequency drift for the transmitter is expected over a specific imaging sequence interval. The frequency of the reference signal is defined as an offset with respect to the center frequency of the scanner, making this technique immune to main field drifts. Following down-conversion, the electrical signal is converted into optical signal for MR-safe transmission. This is also critical to protect the circuitry of the distal unit and receiver from currents that would be induced on the outer surface of the cable.

Thesis No.: 46 Investigation of Oscillatory Mechanisms and Thalamo-Cortical Circuitry of the Visual Systems by Simultaneous EEG-fMRI

Name: Ali Bayram, Year: 2015

Advisor(s): Ahmet Ademoğlu

Abstract: Neural oscillation is an indispensable phenomena in the functioning of the cortical networks. Evoked neural oscillations triggered by external rhythmic stimulation mimic spontaneous ongoing oscillations, thus could shed light on the intrinsic specialization and tuning of the cortical networks. In this thesis, flickering light stimulation is used to constitute steady state for a wide range of temporal frequencies (6-46 Hz) during simultaneous electroencephalography (EEG) and blood oxygenation level dependent (BOLD) functional magnetic resonance imaging (fMRI) scans of 40 healthy volunteers. Firstly, thalamo-cortical loop of the visual system is the subject of interest. Our findings prove that high correlation between the frequency response characteristics of the lateral geniculate nucleus (LGN) and the primary visual cortex (V1) supports the oscillatory tuning property of the thalamo-cortical interactions. Secondly, contribution of oscillations in the modeling of hemodynamic response is discussed based on the sensitivity of BOLD components (phasic and tonic) to temporal frequency. Our results show that, tonic BOLD component is decreasing more sharply than phasic component with increasing frequencies pointing higher dependency of tonic BOLD response to the stimulation frequency. Finally, EEG informed fMRI analysis is conducted for the sake of testing resonance phenomena. The correlation maps between the BOLD responses and the steady state visually evoked potential (SSVEP) amplitudes show significant correlation for the beta and gamma bands but not for alpha band. This result supports the view that the global amplitude maximum of the SSVEP in the alpha band is due to the synchronization without synaptic activity (BOLD) increase.

Thesis No.: 45 Monitoring Depth Of Anethesia Through Measurement of Phase Coupling among Spontaneous EEG Rhythms

Name: Seyed Mortaza Mousavi, Year: 2015

Advisor(s): Ahmet Ademoğlu / Mahrokh.G.Shayesteh

Abstract: Awareness during general anesthesia for its serious psychological effects on patients and some juristically problems for anesthetists has been an important challenge during past decades. Monitoring depth of anesthesia is a fundamental solution to this problem. Induction of anesthesia alter frequency and mean of amplitudes of the electroencephalogram (EEG), and its phase couplings. By increasing the anesthetic drug dose, the mean frequency of the signal decreases and its amplitude increases and theta or delta waves appear. In this study, we analyze EEG changes for phase coupling between delta and alpha sub-bands using a new algorithm for depth of general anesthesia (DOA) measurement based on complex wavelet transform in patients anesthetized through total intravenous anesthesia (TIVA) by Propofol. By taking bispectral index (BIS) values as reference we calculate entropy and histogram of modulated signals.Entropies correspond to different BIS intervals using Mann-Whitney U test show that they have different continuous distributions.The results demonstrate that there is a phase coupling between 3-4 Hz in delta and 8-9 Hz in alpha sub-bands and these changes are shown better at the channel (T7) of EEG. Moreover, when BIS values increase, the entropy value of modulated signal also increases and vice versa.Measuring phase coupling between delta and alpha sub-bands of EEG signals through Morlet continuous complex wavelet transform analysis reveals the depth of anesthesia level.The method can be used to measure depth of general anesthesia to prevent awareness of the patients during anesthesia.

Thesis No.: 44 Antibacraterial Photodynamic Therapy with Indocyanine Green and Near-Infrared Light

Name: Nermin Topaloğlu, Year: 2014

Advisor(s): Murat Gülsoy/Şahru Yüksel

Abstract: Increase in antibiotic-resistance is a worldwide health problem which may result in septicemia and subsequent death in recent years. Some of these deaths are caused by nosocomial, burn or chronic wound infections. Photodynamic therapy can be an alternative technique in treatment of infections. This research aimed to investigate the bactericidal effect of photodynamic therapy with indocyanine green and near-infrared light in vitro and in vivo. First, the effect of indocyanine green and 809-nm laser light was examined on wild type and resistant strains of Staphylococcus aureus and Pseudomonas aeruginosa in vitro. Indocyanine green concentration and laser dose were initially optimized for wild type strains. After determining most effective concentrations with specified light dose, they were applied on resistant strains. This method was totally efficient to kill these strains and optimum doses varied with different strains. Later, this method was examined on rat excisional and abrasion wound models. Wounds were infected by resistant strains of S. aureus and P. aeruginosa. Optimum parameters could not be found for excisional wounds because of bleeding, but infected abrasion wounds could be successfully treated. Around 90% reduction in bacterial burden was observed. Applied energy dose did not cause any thermal damage on healthy tissue.

Thesis No.: 43 MRI Assesment of in vivo Epimuscular Myofascial Force Transmission

Name: Alper Yaman, Year: 2014

Advisor(s): Cengizhan Öztürk/Can Yücesoy

Abstract: Recent developments have been evolving magnetic resonance imaging (MRI) to a combined tool in order to assess human anatomy and physiology in vivo. In the present thesis 3D high resolution anatomic and diffusion weighted imaging capabilities of MRI were combined with nonrigid registration technique in order to quantify principal strains and fiber direction strains locally. The presented method was used to assess the effects of epimuscular myofascial force transmission (EMFT) and external mechanical load simulating ischemic compression manual therapy technique in human lower leg in vivo. In healthy subjects, global length changes of gastrocnemius muscle-tendon complex were shown to cause sizable and heterogeneous local principal strains and fiber direction strains within the all muscles of the limb. It was concluded that EMFT has determinant role in human muscles that affects the mechanical characteristics of synergistic and antagonistic muscles as changing heterogeneity of fiber lengths. Thus it was proven that muscles are not isolated functioning units in vivo. Even all muscles of lower leg were kept isometric, external mechanical load imposed on gastrocnemius muscle caused pronounced and quite heterogeneous principal strains not only within that muscle but also in other muscles of the limb. These findings may lead therapists to relate the mechanical load and the size and penetration of deformations it creates.

Thesis No.: 42 Time-Frequency and Time-Scale Analysis of Non-Stationary Biomedical Signals

Name: Görkem Serbest, Year: 2014

Advisor(s): Yasemin Kahya/Halil Özcan Gülçür

Abstract: Fourier transform (FT), which assumes that the analyzed signal is stationary, is not entirely appropriate to analyze biomedical signals since they are in non-stationary nature. To overcome this drawback, FT can be applied over short-windows of time within which the signal can be considered to be stationary. However, this short-time Fourier transform is hampered with a serious time-frequency (TF) trade-off dilemma. Recently, a number of different TF analysis techniques has been developed that provide improved TF resolution. In this dissertation, we consider two strongly non-stationary biomedical signals, lung sound and blood-flow signals, and propose novel and effective systems for the detection of crackles from the former and emboli from the latter. The crackle detection system uses the dual tree complex wavelet transform (DTCWT) for denoising and time-frequency/scale analysis with various windows/wavelets for feature extraction. The emboli detection system processes forward and reverse flow signals using FT, discrete wavelet transform (DWT), and DTCWT. Dimensionality of the extracted coeffcients is reduced using Principal Component Analysis, and the new features are used for predicting whether a signal is emboli, speckle or artifact. Since the dyadic TF tiling of classical DWT is not appropriate for processing embolic signals, and since the discrete wavelet packet transform (DWPT) can adaptively decompose the TF axis, we also propose a directional complex DWPT for mapping directional information while processing quadrature signals (QSs). This method has significantly less computational complexity than the existing methods. To overcome the poor frequency resolution, severe frequency aliasing and lack of shiftinvariance drawbacks of the DWT, we also propose a novel directional complex DWT. It consists of filterbanks with rational sampling factors and can be applied directly to QSs.

Thesis No.: 41 An Fmrı Based Method For Characterizing Superficial Layer Contamination in Fnırs Signals

Name: Sinem Burcu Erdoğan, Year: 2014

Advisor(s): Ata Akın /Yekta Ülgen

Abstract: Functional near infrared spectroscopy (fNIRS) is a method for monitoring cerebral hemodynamics with a wide range of clinical applications. fNIRS signals are contaminated with systemic physiological interferences from both the brain and superficial tissues, resulting in a poor estimation of the task related neuronal activation. In this study, we introduce an extended superficial signal regression (ESSR) method for cancelling physiology-based systemic interference in fNIRS signals. We apply and validate our method on the optically weighted BOLD signals, which are obtained by projecting the fMRI image onto optical measurement space by use of the optical forward problem. The performance of ESSR method in removing physiological artifacts is compared to i) a global signal regression (GSR) method and ii) a superficial signal regression (SSR) method. The retrieved signals from each method are compared with the neural signals that represent the "ground truth" brain activation cleaned from cerebral systemic fluctuations. We report significant improvements in the recovery of task induced neural activation with the ESSR method when compared to the other two methods with higher spatial localization, lower inter-trial variability, and higher contrast-to-noise (CNR) improvement. Our findings suggest that, during a cognitive task i) superficial scalp contribution to fNIRS signals varies significantly among different regions on the forehead and ii) using an average scalp measurement together with a local measure of superficial hemodynamics better accounts for the total systemic interference. We conclude that maximizing the overlap between the optical pathlength of superficial and deeper penetration measurements is of crucial importance for accurate recovery of the evoked hemodynamic response in fNIRS recordings.

Thesis No.: 40 Detection And Assesment of Cardiac Patent Foramen Ovale

Name: İsmail Burak Parlak, Year: 2013

Advisor(s): Ahmet Ademoğlu

Abstract: Arterial microemboli are gas filled structures which are formed in intravascular and extravascular environment. They are characterized in spherical or ellipsoid forms which would cause diseases in a broad range from stroke to migraine. Cardiac Patent Foramen Ovale (CPFO) is considered as a congenital defect through both atria as a permeable shunt with a prevalence frequency of 25-30% in asymptomatic population. Decompression Sickness (DCS) is a fatal disease during hyperbaric and hypobaric ac- tivities due to unestimated effects of microemboli. CPFO aperture combined with DCS is a clinical problem where bubble analysis is managed manually by special and trained cardiologists. Even this problem was considered recently by different groups within sound, image and video forms, an automated tool is considered as a challenge due to algorithmic and mechanical constraints related to noise, monitoring and probe localization. We aimed to develop a spatio-temporal methodology for clinicians which would not carry out long lasting videos where the number and the size of microemboli alter dynamically. In this thesis, developed methods are classified into two groups; qualitative and quantitative assessments. These approaches were tested initially in a simulation environment with artificial microemboli. Furthermore, microemboli and CPFO were monitored in subjects through videos using two modalities: contrast Trans Esophageal Echocardiography and contrast Trans Thoracic Echocardiography. Even our procedures would get accurate findings within videos, it is important to note that low resolution, high speckle noise, shadowing would introduce false alarms. Conse- quently, we conclude that this routine would standardize CPFO analysis and offer better adjustment for bubble detection.

Thesis No.: 39 Revealing Gene Interactions Using Bayesian Networks

Name: Şenol İşçi, Year: 2013

Advisor(s): Cengizhan Öztürk

Abstract: High throughput biological data (HTBD) targeting understanding of biochemical interactions in the cell can best be analyzed, and explained within the context of networks and pathways. Such data generally represents stochastic nonlinear relations embedded in noise. Bayesian Network (BN) theory provides a framework to analyze the data regarding gene regulation measurements, as this framework naturally handles the aforementioned obstacles. In this dissertation, we provide a two faceted approach to the applications of BNs to HTBD. In the first facet, a novel method is provided, which models known biological pathways as BNs, and uses given HTBD to find pathways that best explain underlying interactions. During this process, biological pathways are converted to directed acyclic graphs, and a score measuring fitness of the observed HTBD to a given network is calculated. Statistical significance of these scores is assessed by "randomization via bootstrapping", and relevant pathways are identified with a certainty that can be used as a comparative measure. Simulations using synthetic and real data demonstrated robustness of the proposed approach, called Bayesian Pathway Analysis (BPA). BPA provides improvement over existing similar approaches by not considering genes in a pathway simply as a list, but incorporating to its model the topology via which genes in a given pathway interact with each other. Although network learning techniques are very useful to reveal the underlying biological phenomena with the help of HTBD, these techniques do not always perform well. This is due to the problems created by the small number of samples, inconvenient initial choice for the network structures, noise inherent in the data, and the complexity of the networks. To improve their performance, the learning techniques can be supported by prior biological knowledge, which are already verified by experimental assays. In the second facet explored in this dissertation, we established a global approach to integrate known biological information to Bayesian learning in order to reveal gene interactions. The proposed framework makes use of external biological knowledge to predict if two given genes interact with each other. To this end, prior knowledge about interaction of two genes is utilized by generating a Bayesian Network Prior (BNP) model, using existing external biological knowledge. External knowledge types to be utilized were obtained from interaction databases such as BioGrid and Reactome, and consist of protein-protein, protein- DNA/RNA, and gene interactions. The resulting model is incorporated into greedy search algorithm for learning networks from HTBD, and interacting genes are represented in the form of a network. In this process of net- work generation, the BNP model deducing gene interactions from external knowledge are used to calculate the probability of candidate networks to enhance the structure learning task. Simulations on both synthetic and real data sets showed that the pro- posed framework can successfully enhance identification of the true network, and be used in predicting gene interactions.,

Thesis No.: 38 Diffusion Tensor Fiber Tracking with Self - Organizing Feature Maps

Name: Dilek Göksel Duru, Year: 2013

Advisor(s): Mehmed Özkan

Abstract: The diffusion tensor imaging (DTI) is unique in its ability to estimate the white matter (WM) fiber tracts in vivo noninvasively. The post-processing of DT images needs proper image analysis and visualization tools. However, accurate WM anatomical maps should be provided to clarify the multiple orientational fiber paths within uncertainty regions. These regions with intersecting trajectories generate a critical tractography issue in DTI literature. WM fiber tractography needs a standard- ization, a generally accepted fiber tract atlas which is the main concern of the various research groups in the field. In this thesis, the special class of artificial neural networks (ANN) namely Kohonen's self organizing feature maps (SOFMs) is proposed for the analysis of DT images. This SOM based tractography approach called SOFMAT (Self-Organizing Feature Mapping Tractography) relies on unsupervised learning method for the mapping of high dimensional data into a 1D, 2D, or higher dimensional data space depending on the topological ordering constraint. The unsupervised approach enables SOFMAT to order the principal diffusivity of the fibers in the DTI into neural pathways. A major advantage of the topological maps produced by SOFMAT is that it retains the underlying structure of the input space, while the dimensionality of the input space is reduced. As a result, an artificial neuronal map is obtained with weights encoding the stationary probability density function of the input pattern vectors. Building fiber tracking maps based on the diffusion tensor information which learn through self or- ganization in a neurobiologically aspect is the aim of the study. SOFMAT has been tested to reveal uncertainties in fiber tracking. A well known artificial dataset called PISTE was used to access the capabilities of SOFMAT. After identifying an affective configuration, SOFMAT was employed for human tractography.

Thesis No.: 37 Clinical Grade Active Guidewire Design for Cardiovascular Interventional MRI

Name: Merdim Sönmez, Year: 2013

Advisor(s): Özgür Kocatürl

Abstract: In cardiovascular interventions, magnetic resonance imaging (MRI) can be used as an alternative to X-ray fluoroscopy to address problems such as soft tissue contrast and exposed ionized radiation. In recent years, advances in imaging techniques and innovative procedures have increased interest in using MRI guidance for minimally invasive procedure. An increasing number of procedures have been carried out on animals and quite a few studies have been conducted on humans. However, to accomplish a complete transition of MRI-guided therapies and treatments from animal experiments to clinic applications, some challenges need to be overcome. Chief among them is the fact that MRI-guided interventional procedures remain limited by a lack of availability of MR-compatible interventional instruments. In this study, the main goal is to close the gap between investigational studies in animal and clinical applications. First, an MRI-compatible active guidewire for a clinical application was designed and tested. A 0.035″ (128cm in length) active guidewire for MRI right and left heart catheterization at 1.5 T was manufactured in an ISO class 7 cleanroom. The design involved an internal fiber-optic temperature probe to monitor real-time temperature increases at the hottest spot of the guidewire to ensure patient safety during MRI scan. A solenoid coil at the distal end of the guidewire was also attached to change the current distribution of the guidewire and to create a conspicuous tip signal. Visualization of the exact location of the guidewire tip enhanced the safety and effectiveness of the right and left heart catheterization. And the mechanical requirements of the guidewire for right and left heart catheterization were met by using a taper nitinol wire as a core structure and thermoplastic elastomer material to support the entire structure. Second, the safety and effectiveness of the guidewire were evaluated through bench-top tests. The mechanical characteristics of the guidewire were compared to those of commercial counterparts. The guidewire design was modified until the mechanical requirements were met. The signal-to-noise ratio and imaging artifact were measured to evaluate the visibility of the guidewire. And a comprehensive in vitro heating test was conducted in an acrylic box filled with gel simulating human tissue conductivity. The longitudinal heating profile of the whole guidewire was acquired during these tests. In addition, the electrical safety of the guidewire was addressed by designing a leakage current blocking circuit to limit the leakage current. The preclinical in vivo studies were designed and conducted in swine animal models to assess the feasibility of the guidewire during right and left heart catheteri- zation. The studies complied with Good Laboratory Practice (GLP) standards. The guidewire was navigated through the vascular structure and chamber of the heart and used to support the diagnostic catheter. Extensive heating tests were performed to evaluate the heating risk of the guidewire. It was determined that guidewire visual- ization and mechanical properties were suffcient to complete all the steps during the procedures. Finally, a proportional-integral-derivative (PID) controller was implemented to control the scan parameters during the MRI-guided procedure to ensure patient safety. The main aim was to reduce RF induced heating by dynamically adjusting the flip angle based on real- time temperature values coming from the guidewire shaft.

Thesis No.: 36 Effects of Mechanical and Temporal Parameters on Tactile Psychophysical Responses

Name: Mustafa Zahid Yıldız, Year: 2013

Advisor(s): Burak Güçlü

Abstract: Tactile feedback is becoming more important in clinical devices and engineering. Therefore, studies on basic sensory processing in the somatosensory system are essential. In this thesis, the mechanical and temporal parameters affecting the absolute tactile detection threshold of human Pacinian (P) channel were investigated. Temporal summation in P channel was found to be independent of stimulus frequency and the experimental results did not t the classical model of temporal summation. The model needs to be modeled to show the U-shaped Pacinian channel behavior. Additionally, the spatial summation property of the P channel was demonstrated on fingertip at three different contact locations and at three contactor sizes. The effects of skin mechanics on psychophysical thresholds of the P channel were studied by measuring mechanical impedance. A significant correlation was found between the thresholds and the dynamic modulus of the skin. Conventionally, somatosensory evoked potentials (SEPs) are measured on the scalp by applying electrically stimulating the peripheral nerves in the clinical setting. Here, SEPs were represented by different types of wavelet functions, which can be used in data compression. Non invasive recordings of scalp potentials were also investigated by applying strong mechanical stimulation on the fingertip. However, time-frequency analysis did not show much useful information about stimulus properties, which would be useful in understanding basic somatosensory processes. The results of this thesis may be useful in various fields such as haptics, robotics, prostheses, dermatology, and cosmetics. Specifically, spatial and temporal summation should be incorporated in the high-frequency vibrotactile feedback in prosthetic arms.

Thesis No.: 35 Mechanics of Spastic Muscle and Effects of Treatment Technioues: Assessments with Intra-Operative and Animal Experiments

Name: Filiz Ateş, Year: 2013

Advisor(s): Can Yücesoy

Abstract: Present thesis is focused on mechanics of spastic human muscles and the effects of widely used treatment methods in the context of the determinant role of epimuscu- lar myofascial force transmission (EMFT). A novel intra-operative method was devel- oped to measure human Gracilis (GRA) muscle isometric forces with respect to knee angle. In healthy subjects, GRA was shown to have very large operational length range. For spastic cerebral palsy patients on the other hand, GRA muscle did not show “abnormal” mechanical characteristics: (i) Length range was not narrowed and (ii) high flexion forces were not available. Such abnormality occurred if its antago- nist vastus medialis is activated simultaneously. Therefore, EMFT mechanism through inter-antagonistic interaction was suggested to determine human muscle characteristics in spasticity. Effects of treatment methods were investigated in animal experiments: (1) Muscle lengthening surgery was shown to a ect (i) proximal and distal sides differ- entially and (ii) non- operated neighboring muscle as well. (2) Botulinum Toxin Type-A (BTX-A) administration was shown to change the mechanics of not only the injected but also non-injected muscles in conditions close to in vivo. Additional to active force reductions (i) the narrowed length range of force exertion and (ii) pronounced passive force increase contradictory to the aim were shown. EMFT mechanism was concluded to be determinant for the treatment methods as well.

Thesis No.: 34 Neuroimaging of Brain Activity Using Spatio -Temporal Signal Modelling

Name: Adil Deniz Duru, Year: 2012

Advisor(s): Ahmet Ademoğlu

Abstract: Functional neuroimaging enables us to obtain information about how the brain responds to cognitive and/or emotional tasks. Neuroimaging of brain activity requires spatio-temporal modeling of measured electrical and/or hemodynamic data and integration of the measurements obtained at different spatial and or temporal scales. In this thesis, new techniques are employed for the investigation of spatio- temporal dynamics of different functional data as the EEG-ERP, the invasive/non-noninvasive recordings of epileptic EEG, and simultaneously recorded steady state EEG- fMRI. Spatio-temporal wavelet decompositions using realistic head models are applied in order to produce simple stationary input subtopographies for the source localization. Besides, a spatial decomposition method based on radial basis functions is used. The usage of the subtopographies facilitate the inverse solution and it is shown that even the temporally correlated EEG sources can be localized by this approach. Integration of the data obtained from different spatial scales is an important problem in epileptic EEG. To assess their reliability, the spatial performance of the scalp EEG based inverse solutions are compared with deep or cortical measurements and their simultaneously measured datasets. The multimodal functional information integration is proposed to compare the dynamics deduced by the simultaneously recorded SSVEP and fMRI. The temporal correlation between the time series of EEG and fMRI is calculated via the GLM. It is observed that the SSVEP source maps are the spatial subsets of the fMRI activity. The study demonstrates the applicability and potential of new spatio-temporal methods in EEG research which can be used to study cognition, attention, memory, and perception. Proposed methods can also be used as tools in more practical areas like brain computer interfacing, neurosurgical planning and neuro-psychological assessment of certain disorders.

Thesis No.: 33 Design and Development of Thulium Laser System for Medical Applications

Name: Temel Bilici, Year: 2012

Advisor(s): Murat Gülsoy

Abstract: The Thulium (Tm: YAP) laser is suitable for medical applications due to strong absorption in water. In this thesis, a computer controlled Tm: YAP laser system with a power output up to 1 W and emission wavelength of 1980 nm were established. Once the laser system was stabilized, its output power, spot size, and light intensity measurements were performed. The thermal effects of the laser system on brain, liver, heart, and kidney tissues were macroscopically analyzed. The ablation efficiency of the laser system was experimentally tested on ex-vivo brain tissue. The maximum ablation eficiency was obtained at a power level of 200 mW with duration of 10 seconds (69 W/cm2). The fluence effect for skin ablation was analyzed by histology on Wistar rat skin tissues during a 4- day healing period. Temperature measurements by thermal camera and thermocouples were investigated to see the temperature effect of CW and modulated mode of the Tm: YAP laser under skin and on skin surface. The temperature increase was faster and the temperature decrease was found slower in CW mode. The main aim of the study is to explore the welding capabilities of Tm: YAP laser in modulated and CW modes of operation on Wistar rat skin during 21-day healing period. Full- thickness incisions were welded at 100 mW and 5 s (34.6 W/cm2). The results were compared to conventional suture techniques by both histology and tensile strength measurements. After day 4, full closure was obtained for both laser modes, whereas, full closure was not observed till day 4 in suture group. In tensile strength analysis, tensile forces found for both modulated and CW modes of operation were significantly higher than the tensile force values found for conventional suture technique. Tm: YAP laser tissue welding possessed significantly stronger closure than conventional suture technique.

Thesis No.: 32 Skin Tissue Welding With Near Infrared Lasers: Investigation Of The Optimal Parameters

Name: Haşim Özgür Tabakoğlu, Year: 2010

Advisor(s): Murat Gülsoy

Abstract: Laser tissue welding/soldering is an alternative to conventional closure techniques in surgery. In the present study, the closure capability and the contribution to recovery period of laser welding techniques were investigated through comparative experiments. Effects of three near infrared (NIR) wavelengths, 809 nm diode laser, 980 nm diode laser and 1070 nm ytterbium ber laser, were compared not only among themselves but also with classical manual suturing for skin closure competency. Lasers with different NIR wavelengths were delivered to skin incisions via optical bers and laser power was adjusted according to predosimetry studies. In dosimetry experiments all the three NIR lasers were tested for their efficacy in welding; besides, 809 nm diode laser was also tested for its efficacy in laser soldering. Effects of 980 nm laser welding at same energy but different irradiation levels were also compared. Throughout this period, healing was inspected at particular days (1, 4, 7, 14, 21) by histological and mechanical methods. Skin samples were stained with Hematoxylin and Eosin (H&E) in order to assess gross pathological changes along epidermis and dermis created either by photothermal laser tissue interactions or suturing and suture material itself. These changes were quantified as closure index (CI), thermally altered area (TAA), granulation area (GA) and epidermal thickness (ET) by using different microscopy techniques such as brightfield, polarized light and phase contrast. The laser welding techniques were found reliable in terms of immediate and mechanically strong closure compared to suturing.

Thesis No.: 31 Photofrin And Indoocyanine Green-Mediated Photodynamic Therapy In Cancer Treatment

Name: Özgüncem Bozkulak, Year: 2010

Advisor(s): Murat Gülsoy

Abstract: Photodynamic therapy (PDT) is a minimally invasive therapeutic approach for clinical treatment of cancer. PDT-mediated oxidative stress leads to cell death and can elicit the expression of genes associated with cell survival, such as AKT/protein kinase B. Phosphorylation and subsequent activation of AKT induces a survival response. For the first time in literature, our results from in vitro and in vivo experiments demonstrated that PDT treatments mediated by excitation of Photofrin with a 630-nm diode laser induced AKT phosphorylation. PDT-mediated AKT pathway activation may stimulate cell survival in remaining tumor tissue leading to tumor reoccurrence, therefore, inhibiting PDT-mediated AKT activation may improve treatment responsiveness. Our findings demonstrated that, minimally toxic AKT inhibitor, PI- 103, e actively inhibited PDT-mediated AKT phosphorylation both in vitro and in vivo. These results have great importance in relevance to development of combinatorial therapies using PDT and PI-103 inhibitor to improve treatment responsiveness. Indocyanine Green (ICG) exhibits maximum absorption at around 800 nm, which is an advantage for its use in treatment of deeper tumors. In this study, an 809 nm diode laser was designed and custom manufactured in our laboratory to investigate the effects of ICG-mediated PDT on human breast cancer cells. This study for the first time reported that ICG-PDT application exhibited strong and stable phototoxic e effects on MDA-MB231 breast cancer cells. Collectively, these novel findings presented in this thesis study contributed largely to the knowledge of PDT in cancer treatment, which is the first reported PDT study in Turkey, and open new research areas for further investigations.

Thesis No.: 30 A Neuravascular Coupling Model Based On Nitric Oxide And Carbon Dioxide And Its Valisation With Two-Ohoton Microscopy Imaging

Name: Ayşe Meryem Yücel, Year: 2010

Advisor(s): Ata Akın

Abstract: Understanding neurovascular coupling is of paramount importance since while a normal coupling is vital for a healthy functioning brain, the impairment in coupling is the underlying factor of many neurodegenerative diseases. With this motivation, we aimed to test the still-debatable hypotheses and important aspects of neurovascular coupling: whether the coupling is controlled metabolically or neurogenically, how the coupling is propagated, what kinetics the cerebral metabolic rate of oxygen (CMRO2) follows during neuronal activity and the transient characteristics of the response during stimulus and after stimulus periods. We have modified recent models of neurovascular coupling adding the effects of both nitric oxide (NO) kinetics, a well-known neurogenic vasodilator, and CO2 kinetics as a metabolic vasodilator to test the neurogenic and metabolic hypotheses. Using 2-photon microscopy imaging, we measured the vessel diameter changes in vivo in somatosensory cortex of Sprague Dawley rats during forepaw stimulation to investigate response transients and to test retrograde dilation hypothesis. Our results show that the dominant factor in the hemodynamic response is NO, however CO2 is important in modulating the shape of the response: causing post-stimulus undershoot due to the washout effect of cerebral blood flow (CBF) resulting in hypocapnia. The statistical analysis of our experimental results and their comparison with the modeling results give more insight into the transient characteristics of the response. Our results support retrograde dilation hypothesis and suggests a CMRO2 onset and return kinetics in seconds rather than in minutes during functional activity.

Thesis No.: 29 Clinical Grade Active Guidewire And Catheter For Interventional Cardiovascular MRI

Name: Özgür Kocatürk, Year: 2009

Advisor(s): Cengizhan Öztürk

Abstract: The success and safety of interventional magnetic resonance imaging (MRI) procedures requires conspicuous intravascular instruments that can be distinguished from surrounding tissues. In this dissertation work, an "active" (receiver-coil) clinical grade vascular guidewire and guiding catheter were developed with enhanced visibility and favorable mechanical characteristics for MRI guided cardiovascular interventions. Both 0.035-inch guidewire and 7 Fr guiding catheter were designed combining two different antenna designs on independent channels. The devices incorporate a loop antenna to visualize the tip and determine orientation, and a dipole antenna to visualize the whole guidewire shaft. The MRI visibility performance and RF safety tests were performed at 1.5T in vitro and in vivo in swine. The two channel active guidewire design provided accurate tip position information with 0.97 0.42 mm and novel active shaft visibility technique was introduced to polymer based guiding catheter successfully without sacrificing device size or handling. Mechanical testing comparison with several commercially-available guidewires demonstrated that the new guidewire design provides the desired stiffer distal tip, moderate torquability, and pushability suitable for vascular applications. The RF power threshold and limitations were determined to provide reasonable amount of heating during MRI examination. This may enable a range of interventional procedures using real-time MRI.

Thesis No.: 28 Investigation Of The Alterations In Motor Units In Neurologic Disorders By Scanning Electromyography

Name: İmran Göker, Year: 2009

Advisor(s): Yekta ülgen

Abstract: In this study, the alterations in the length of cross-sections of MU and the changes in maximum amplitude of MUAPs in each MU in patients with JME were investigated. An experimental setup of scanning EMG was built and 3-D cross sectional maps of the MUs were plotted in order to measure the length of cross-sections and to find the maximum amplitude of each MU. Three subject groups comprising nine patients with juvenile myoclonic epilepsy as JME group, ten healthy volunteers as normal control (NC) group and three patients with spinal muscular atrophy as SMA group were included. The age of the subjects ranged between 22 and 46. Five to eight measurements were performed from the biceps brachialis muscles of each subject. Data including 113 measurements in total acquired from with these measurements were stored in a computer and then were used to construct 3-D maps of MU territories. All three groups were compared in pairs by using 113 measurements with Student's t-test. JME groups were found similar to SMA group in terms of both parameters. The difference between JME and NC groups was found as extremely significant. Since the increase in both parameters due to the enervation occurs in SMA group, significant difference is expected between SMA and NC group. These results were confirmed with Turkey's HSD test by comparing three groups simultaneously. Three groups were also compared using the individual means of parameters with a non-parametric test such as Mann-Whitney test. A significant difference which is also confirmed again with Turkey's HSD test was found between the JME and NC groups. In conclusion, since no neurogenic evidence was found in JME patients in conventional EMG previously higher length of cross- sections can be considered as structural.

Thesis No.: 27 Advanced Computational Tools For Real-Time MR Imaging

Name: Haris Saybaşılı, Year: 2009

Advisor(s): Cengizhan Öztürk/Ahmet Ademoğlu

Abstract: Real-time Magnetic Resonance Imaging (MRI) has the potential of successfully guiding interventional applications. Overall, the requirements of real-time MRI can be categorized as: (i) fast data acquisition, (ii) fast image reconstruction, and (iii) good image quality. Fast data acquisition is provided by optimized real-time sequences, by parallel MRI (pMRI) techniques, or by non-Cartesian acquisition schemes (e.g. spiral and radial trajectories). However, fast image reconstruction is non- trivial, especially when computations demanding pMRI methods or non-Cartesian trajectories are involved. Even though signal-to-noise ratio (SNR) can be relatively high during real-time imaging, spatial resolution is limited. Thus, improved visual feedback during real-time MRI guided interventions is a must. This thesis defined three specific aims to improve real-time imaging: (i) real- time image reconstruction for pMRI, (ii) real-time image reconstruction for non-Cartesian trajectories, and (iii) fast MRI post-processing for improved visual feedback during interventions. Thesis contributions include: (i) real-time hybrid domain TGRAPPA based pMRI reconstruction algorithm (currently the fastest TGRAPPA based algorithm), (ii) first real-time implementation of GRAPPA Operator Gridding algorithm for radial acquisitions, (iii) multi-phase 3D angiography roadmaps for MRI guided interventions, (iv) improved active device visualization during real- time MRI guided interventions, (v) integration of a real-time active device localizer algorithm.

Thesis No.: 26 Accuracy Improvements Of NIRS And Investigation Of Muscle Oxidative Metabolism

Name: Ömer Şayli, Year: 2009

Advisor(s): Ata Akın

Abstract: In the first part of the thesis, the effect of fat layer on continuous wave near infrared spectroscopy (cw-NIRS) measurements were investigated in detail, both in terms of underestimation error (caused by homogeneous medium assumption) and crosstalk between chromospheres because of homogeneous medium assumption and wavelength dependence of mean partial path length in the muscle layer. These errors have been investigated by Monte Carlo simulations with a skin-fat-muscle layered tissue model for a two wavelength system. The errors have been found to be higher for thicker fat thicknesses. A correction algorithm was proposed with the use of wavelength dependent partial path length in the muscle layer derived with Monte-Carlo simulations. Two detector cw-NIRS system was also analyzed and compared with 1-detector cw- NIRS system. The performance was promising but true assumption of initial optical coefficients of the layers poses a challenge for the performance. Muscle metabolism, fatigue and endurance was examined with usage of three simultaneous measurement modalities: cw-NIRS, SEMG and force-time for isometric hand grip exercise. The study revealed some physiological processes related to fatigue. A highly valued and statistically significant correlations were found between sEMG and cw-NIRS derived parameters especially at 50% maximal voluntary contraction along with biometrics for endurance prediction. These information could be important in sports applications, ergonomics, physical medicine and rehabilitation to monitor the recovery with objective parameters.

Thesis No.: 25 The Effect Of Dialysis Environmet And The Clinical State Of Patients With Chronic Kidney Failure On The High Flux Dialyzers,

Name: Mehmet Emin Aksoy, Year: 2008

Advisor(s): Hikmet Üçışık

Abstract: In order to optimize the renal replacement therapies many researches have been going on for many years. The tendency for dialysis therapy is towards high flux hemodialysis in the last few years. For understanding the behavior of newly designed hollow fibers under high flux dialysis condition, new experiments should be designed. Experiments are designed to study the stability of the two different membranes, polysulfone and polyamide, from high flux dialyzers. Hemodialysis sessions were performed on a group of patients with dialysis ages less than two years and without any other accompanying disease. Microscopical studies performed on virgin and used dialysis membranes showed morphological changes during dialysis session. Mechanical tests revealed the differences in the mechanical properties of virgin and used membranes. The change in the degree of crystallinity of the polysulfone and polyamide membranes during dialysis was observed under X-Ray Diffraction (XRD). It was found that dialysis increases the crystallinity. This issue is very important for dialysis centers performing reuse procedures for dialysis centers, because any damage to dialysis membranes would cause very serious clinical complications. Differential scanning calorimetry (DSC) studies showed structural changes resulted by dialysis. Unlike the other analytical techniques used, the capacity of FTIR did not give enough information. The data obtained in the course of this study showed that high flux dialysis sessions cause irreversible structural changes, which may result in clinical complications during reuse of dialyzers

Thesis No.: 24 Modelling And Clustering Analysis Of Pulmonary Crackles,

Name: Mete Yeğiner, Year: 2008

Advisor(s): Yasemin Kahya

Abstract: The objective of this study is to perform two complementary analyses of pulmonary crackles, i.e. modeling and clustering, in order to interpret crackles in time frequency domain and also determine the optimal number of crackle types and their characteristics using the modeling parameters. Since the crackles are superimposed on background vesicular sounds, a preprocessing method for the elimination of vesicular sounds from crackle waveform is also proposed for achieving accurate parameterization. The proposed modeling method, i.e. the wavelet network modeling, interprets the transient structure of crackles in the time-frequency space with a small number of components using the time-localization property of wavelets. In modeling analysis, complex Morlet wavelets are selected as transfer functions in the hidden nodes due to both their similarity with the crackle waveforms and their exibility in the modeling process. Clustering analysis of crackles probe the discrepancies found among the studies related with the crackle types and their corresponding characteristics. Since, in these studies, crackles are classified according to the auditory perception of the observers, there are inconsistencies found in the labeling of the same crackle. To overcome the inherent subjectivity, the crackles are classified in an unsupervised method using the EM clustering analysis. In this method, it is assumed that the crackle data can be interpreted with the multivariate Gaussian mixture model and, therefore, crackle clusters distribute normally in the feature spaces. The results strongly suggest the existence of a third crackle type, medium, in addition to the commonly used two types, i.e. ne and coarse. Moreover, the extracted characteristics of crackle types offer additional features for the computerized crackle-based analysis of pulmonary disorders.

Thesis No.: 23 Statistical Analysis Of Cognitive Signals Measured by fNIRS,

Name: Rıfat Koray Çiftçi, Year: 2008

Advisor(s): Yasemin Kahya

Abstract: Further standardization in signal processing tools is needed in the area of functional near infrared spectroscopy (fNIRS) before it is recognized as a reliable neuroimaging modality. This thesis study attempts to present a comprehensive analysis of the feasibility of applying statistical inference methods to fNIRS signals. Using hierarchical linear models, both classical and Bayesian techniques are pursued and performances of different methods are presented on a comparative basis. The results obtained from a set of cognitive signals show that fNIRS can identify cognitive activity both at the subject and group levels. The analysis suggests that mixed or Bayesian hierarchical models are especially convenient for fNIRS signals. A related problem that is discussed in this thesis study is to relate the outcome of the statistical analysis with the underlying physiology. This problem is studied by putting constraints over the parameters to be estimated. Carrying the problem to a Bayesian framework, the constraints were turned into prior distributions and Gibbs sampling was used to infer from the posterior distributions. The results exhibit that in addition to preventing unlikely results to appear at the end of the analysis, using parameter constraints is also more efficient in revealing activations which are obscured by heavy noise. The last part of this thesis study departs from hypothesis-based statistical inference techniques and introduces the use of information- theoretic measures for fNIRS by particularly concentrating on neural complexity and functional clustering. It is demonstrated that this type of measures may capture organizational aspects of the brain which are hard to reveal with classical statistical inference techniques.

Thesis No.: 22 TheNanostructural Role Of Water in Lamellar Bone And Its Implications On Osteonal Bone Mechanics: A Micrographic And Opromechanical Study

Name: Feride Şermin Bilgen, Year: 2008

Advisor(s): Hale Saybaşılı

Abstract: The microstructural organization of water in bone was investigated using the environmental scanning electron microscope to analyze the dimensional changes that occur during dehydration of equine osteonal bone. In longitudinal sections, 1.2% contraction perpendicular to the lamellae, 0% parallel to the lamellae; in transverse sections,1.4% contraction both parallel and perpendicular to the lamellae were observed. Scanning electron microscopy back scattered electron images showed that about half of an individual lamella is less mineralized, thus more hydrated, indicating that contractions perpendicular to lamellae are due to the presence of more water-filled rather than mineral-filled channels within the mineralized collagen fibril arrays. As these channels are also aligned with the crystal planes, the crystal arrays facilitate or hinder contraction in different directions. The mineralized collagen fibril arrays, laid down in the form of primary circumferential lamellar bone are replaced with secondary osteonal lamellar bone. The mechanical properties of these two types of lamellar bone are studied to understand how bone functions under load during the remodeling process. Twenty minipig cortical bone samples were tested using an optomechanical testing system. Deformation of tissue after each 2-micrometer compression increment was detected orthogonally in-plane (x,y) and out-of-plane (z). Linear regression of stress and strain of partially remodeled bones gave an E1and v12 of 7.9 ± 2.1 GPa and 0.3. The circumferential lamellar bone had an average E1 of 9.4 ± 2.0 GPa compared to the average E1 of 6.8 ± 0.8 GPa for the osteonal bone.

Thesis No.: 21 Development Of New Orthosis (Neuro-orthosi) for the control of wrist movements in Patients With Carpal Tunnel Syndrome

Name: Ümit Uğurlu, Year: 2008

Advisor(s): Mehmed Özkan

Abstract: Static wrist orthoses (SWOs) are used in carpal tunnel syndrome (CTS) with some drawbacks. As an alternate approach, an active closed-loop wrist control strategy was proposed to limit wrist movements. It was based on the electrical stimulation of antagonistic muscle(s) to prevent motion beyond preset limits. The purposes of the study were to determine whether the proposed “neuro-orthosis” (NeO) system resulted in less restriction in the function and strength of the hand compared to custom-made SWOs and its ability to limit the wrist movements. A case-control study was designed. 31 right-handed volunteers participated in the study. 12 of them were patients with CTS, and the others were healthy subjects. Function, dexterity, and strengths were measured under three different testing conditions: without orthosis, with a SWO, and with the NeO system. Standardized test instruments and test procedures were used for all measurements. Maximum angles at each direction were recorded while the NeO system was on and off. At the end of the SWO and the NeO test conditions the level of discomfort were questioned by means of 10 cm visual analog scale. SWOs caused significant decrements in most of the tests with respect to the noorthosis test condition. The NeO system also led to some limitations in the test scores. However it was found to be less constraining with respect to a SWO. Although the NeO was not able to strictly limit the movements into preset limit, the resulting movement range was still in the safe area. The NeO system resulted in more discomfort in general.

Thesis No.: 20 Mutimodel Investigation of fMRI and fNIRS Derived Breath Hold BOLD Signals with an Expanded Balloon Model

Name: Uzay Emrah Emir, Year: 2008

Advisor(s): Ata Akın /Cengizhan Öztürk

Abstract: Multimodal investigation of blood oxygenation level-dependent (BOLD) signal, using both functional near infrared spectroscopy (fNIRS) and functional magnetic resonance imaging (fMRI), may give further insight to the underlying physiological principles and the detailed transient dynamics of the vascular response. Utilizing a breath hold task (BHT), we measured deoxy-hemoglobin (HbR) and oxy-hemoglobin (HbO) changes via fNIRS and blood oxygen level dependent (BOLD) changes by fMRI. Measurements were taken in four volunteers asynchronously and carefully aligned for comparative analysis. In order to describe the main stimulus in BHT, partial pressure of carbon dioxide (PaCO2) parameter was integrated into the balloon model as the driving function of cerebral blood flow (CBF) which led to the development of an expanded balloon model (EBM). During BHT, the increase in HbR was observed later than the BOLD peak and coincided temporally with its post stimulus undershoot. Further investigation of these transients with PaCO2 integrated balloon model suggests that post stimulus undershoot measured by fMRI is dominated by slow return of cerebral blood volume (CBV). This was confirmed by fNIRS measurements. In addition, BOLD signal decreased with the increase of the initial level of PaCO2 derived from EBM, indicating an effect of basal CBF level on the BOLD signal. In conclusion, a multimodal approach with an appropriate biophysical model gave a comprehensive description of the hemodynamic response during BHT.

Thesis No.: 19 Lesion Detection in MR Mammography: NMITR Maps, Dynamic and Morphological Descriptors

Name: Gökhan Ertaş, Year: 2007

Advisor(s): Halil Özcan Gülçür

Abstract: In this thesis, algorithms, methods and techniques for dynamic contrast-enhanced magnetic resonance mammography (DCE-MRM) have been investigated to maximize sensitivity, specificity and reproducibility of breast cancer diagnoses. A novel lesion localization method that uses cellular neural networks (CNNs) was developed. The breast region was segmented from pre-contrast images using four specifically designed CNNs. A 3D normalized maximum intensity-time ratio (nMITR) map of the segmented breast was generated using a moving mask of 3×3 voxels on the dynamic images. This map was converted into a binary form and processed with a fuzzy CNN consisting of three layers of 11×11 cells to segment out lesions from the surrounding tissues and to filter-out deceptive enhancements. A set of decision rules based on volume and 3D eccentricity of the suspicious regions were applied to minimize false-positive detections. The system was tested on a dataset consisting of 7020 MR mammograms in 1170 slices from 39 patients with 37 malignant and 39 benign mass lesions and was found to perform well with false positive detections of 0.34/lesion, 0.10/slice and 0.67/case at a maximum detection sensitivity of 99%. Enhancement and morphological descriptors of breast lesions derived from 3D nMITR maps were also studied for malignancy detection. The mean, the maximum value, the standard deviation and the entropy were the enhancement features found to have high significance ($P < 0.001$) and diagnostic accuracy (0.86-0.97). nMITR-entropy had the best performance. Among the morphological descriptors studied, 3D convexity, complexity and extent were found to have higher diagnostic accuracies (ranging between 0.70-0.81) and better performance than their 2D versions. Contact surface area ratio was found to be the most significant and accurate descriptor (75% sensitivity, 88% specificity, 89% PPV and 74% NPV). The results demonstrate that nMITR maps inherently suppress enhancements due to normal parenchyma and blood vessels that surround lesions and have natural tolerance to small field homogeneities and thus are very effective for lesion localization and malignancy detection

Thesis No.: 18 Three Dimensional Modelling of Knee Joint: Prediction of Ligament Related Gait Abnormalities

Name: N. Ekin Akalan, Year: 2007

Advisor(s): Mehmed Özkan

Abstract: The purpose of this study is to investigate the affect of anterior bundle of ACL (aACL), anterior portion of posterior cruciate ligament PCL (aPCL), anterior and deep portions of MCL (aMCL, dMCL) and the tibiofemoral articular contacts on to passive knee motion. A well accepted reference model for a normal tibio-femoral joint was reconstructed from the literature in which attachments of the bundles of the ligaments and the articular surfaces in medial and the lateral components were carefully defined. Another three dimensional dynamic tibiofemoral model which includes the isometric fascicles, aACL, aPCL, aMCL, dMCL, and the medial-lateral articular surfaces were represented as the constraints to predict the trajectory of the tibia on the femur during flexion. The tibiofemoral model was also integrated in to the dynamic patella-tibio-femoral model. The behavior of the knee model was also tested by simulating dynamic and static clinical tests such as knee extension exercise and drawing test. The patello- tibio-femoral model was integrated into full-body model to simulate people walk with normal and ACL deficient patterns. The predictions were closely agreed with the literatures and correspond well to measurements of the model which represents natural patello-tibio-femoral joint. The aACL, aPCL, aMCL, dMCL bundles and the medial-lateral articular surfaces might play a primary role to give the nature of distal femoral sphere like shape. The clinical significance of the work is that anything which changes the lengths and locations of the related ligaments may demolish natural constraints and force the articular structures in to unnatural shape which may make the knee to change contact behavior on the articular surface and may cause pain. The surgical treatments must be accurate enough to provide both ligament bundle geometries and articular geometry to achieve a problem free knee kinematics after the surgery.

Thesis No.: 17 Biological Effects of Electromagnetic Fields at Mobile Telecommunication Frequencies

Name: Ali İhsan Yürekli, Year: 2006

Advisor(s): Mehmed Özkan

Abstract: The increasing use of cellular phones and increasing number of base stations are becoming widespread source of non-ionizing electromagnetic radiation. The immediate biological effect of electromagnetic (EM) radiation is the generation of heat in the body and it is generally evident under high levels of electromagnetic energy. However, some biological effects are likely to occur even at low-level EM fields. In this study, a Gigahertz Transverse Electromagnetic (GTEM) test chamber was used as an exposure environment for plane wave conditions of far-field free space EM field propagation at the GSM Base Transceiver Station (BTS) frequency of 945 MHz and effects on oxidative stress in rats were investigated. Groups of young adult male Wistar albino rats were kept inside the test chamber for 7 hours/day for a period of 8 days. When EM fields producing Specific Absorption Rate of 11.3 mW/kg(power density 3.67 Watt/square-meter), which is well below current exposure limits, were applied, MDA (malondialdehyde) level was found to increase and reduced glutathione (GSH)concentration was found to decrease significantly ($p<0.0001$). Additionally, there was a less significant ($p=0.0190$) increase in SOD (superoxide dismutase) activity under EM exposure, when compared to the sham exposed group. Leukocyte counts before and after the experiment and vanil mandelic acid (VMA) levels during the experiment were also assessed. We conclude that free radical mechanisms may have a probable role on the adverse effects of EM fields at mobile telecommunication frequencies.

Thesis No.: 16 3-D Gamma Knife Dose Distribution by Normoxic Gel Dosimetry Near Tissue Inhomogeneties

Name: Fatih İşbakan, Year: 2005

Advisor(s): Yekta ülgen

Abstract: The primary goal in this study was to investigate the three dimensional dose distributions, near the areas of tissue inhomogeneities, in Gamma Knife Radiosurgery with the normoxic gel dosimetry. Following irradiation, when scanned in MR and post processing the MR images, dose imparted to any particular point in the gel phantom can be calculated via the true T2 relaxation time at that point. In the neighborhood of air-tissue inhomogeneity in the head, electronic disequilibrium can lead to errors in dose calculated with the treatment planning algorithms that presume the head as a homogeneous media. Two experiments were designed to investigate the inhomogeneity effects in the Gamma Knife radiosurgery: one experiment simulating the volume near the auditory canal cavity and, the other simulating the volume near the paranosal sinuses cavity. In the auditory canal cavity experiment, an identical balloon of a diameter of 16 cm with two corks placed on each side to represent the air cavities constitutes the inhomogeneous phantom. In the paranosal sinuses cavity experiment, a cylindrical cork is placed to represent the maximal sinuses. In both experiments, the homo geneous phantom is a spherical glass balloon filled with normoxic polymer gel. For dose calibrations, 100 ml vials filled with the same gel are irradiated at predefined doses, and the R2- dose calibration curve is extracted. Dose distributions are the results of a single shot, by using all 201 Cobalt sources, delivered to a known point in the phantoms. In the aspect of dosimetrical quality control, the Gamma Knife planning system predicted dose distribution is compared with the experimental results. In the homogeneous phantoms, the gel dosimetry calculated dose distribution is in good agreement with the Gamma Plan predicted dose distribution. However, in the case of inhomogeneous phantoms, the dose distribution is spatially different and significant differences in dose levels are observed. The dose decrease near the air-tissue interface causes the overshooting of the dose by the Gamma Plan. This underdosing effect can be essential for the lesions near tissue inhomogeneities. In the auditory canal cavity experiment, the diameter of the 50% isodose curves differ by 35% in the X axis and 1% in the Y axis for Z=105 mm axial plane; and by 39% in the X axis and 5% in the Z axis for Y=105 mm coronal plane in the inhomogeneous phantom as compared to the homogeneous phantom. In the paranosal sinuses cavity experiment, the diameter of the 50% isodose curves differ by 42% in the X axis and 47 %in the Y axis for Z=71mm axial plane; 42% in the X axis and 60%in the Y axis for Z=75 mm axial plane; 52% in the X axis and 70% in the Y axis for Z=79 mm axial plane respectively in the inhomogeneous phantom when compared to the homogeneous phantom. The dose decrease near the air tissue interface causes the Gamma Plan’s predicted dosage to be higher than that actually delivered. The resulting underdosing effect can be critical for the control of the lesions near tissue inhomogeneities.

Thesis No.: 15 Modeling of Physiological Propertis of Stored Human Blood by Complex Impedance Measurements

Name: Mana Sezdi, Year: 2005

Advisor(s): Yekta ülgen

Abstract: In this study, the relationship between physiological properties of human blood, namely Na+, K+, Cl- concentrations, pH, 2,3-DPG and ATP, and its electrical parameters, the Cole-Cole parameters- the resistance of the extracellular fluid (Re), the resistance of the red cell interior fluid (Ri), phase angle, characteristic frequency (Fc) and the capacitance of the cell membranes (Cm)- is investigated. Measurements are performed on 51 erythrocyte suspension (ES) samples, subject to42 days of storage at 4oC, on day 0, 10, 21, 35 and 42. On whole blood (WB) samples (31 samples) under 21 days of storage, same measurements are done on day 0, 10 and 21.Electrical measurements are performed in the frequency range from 100 kHz to 1 MHz at room temperature. Multifrequency complex impedance data are fitted to Cole-Cole diagrams using Least Mean Square algorithm to give Cole-Cole parameters for the equivalent electrical circuit model of blood samples. Variance analysis (ANOVA test) is used to evaluate differences in blood properties relative to storage time. The relationship between the physiological and the electrical parameters of blood is investigated by regression analysis using SPSS. A multiple regression model is developed for ES and WB separately, where the physiological parameters are expressed in terms of the electrical parameters. In a case study, the models are tested for 20 donors, and it is seen that the model for WB is appropriate for predicting Na+, K+, Cl-, pH and ATP at all time, for ES the model is only appropriate for the first 35 storage days. The models cannot estimate 2,3-DPG at all, at any time. This study clearly showed that complex impedance measurement technique can be a valuable tool in predicting the viability of stored blood.

Thesis No.: 14 Modeling and Analysis of the Interaction Between Renal Sympathetic Nerve Activity, Arterial Pressure and Sodium Excretion.

Name: Fatih Karaaslan, Year: 2004

Advisor(s): Yağmur Denizhan

Abstract: High basal renal sympathetic nerve activity (rsna) is known to contribute to the pathogenesis of hypertension, congestive heart failure, nephrotic syndrome and hepatic cirrhosis. Because of this clinical importance of rsna a mathematical model has been developed, which allows the long-term analysis of the effect of rsna on arterial pressure and sodium excretion. Previous long- term cardiovascular models in the literature do not explicitly include most of the effects of rsna on kidney functions. Some of them take only the effect of the rsna on renal vascular resistance into account. In this dissertation, a long-term cardiovascular system model is presented that integrates the previous models developed by Guyton, Uttamsingh and Coleman. Additionally it introduces mechanisms of direct rsna effects on tubular sodium reabsorption and renin secretion in accordance with experimental data from literature. The resulting mathematical model constitutes the first long- term model of the cardiovascular system accounting for the effects of the rsna on kidney functions in such detail. Simulations of test situations have revealed that the closed loop behavior of the model sufficiently resembles clinical and experimental results available in the literature, in terms of basic cardiovascular and renal dynamics. The model not only provides an understanding of renal sympathetic nerve activity-increase-related mechanisms which give rise to an increase in mean arterial pressure in case of hypertension and to an increase in the total sodium amount in cases of congestive heart failure, nephrotic syndrome and in cirrhosis. It also accounts for mechanisms, which, due to the impairment of renal sympathetic nerve activity inhibition under sodium loading, rise the mean arterial pressure in salt-sensitive hypertension and the total sodium amount in congestive heart failure, nephrotic syndrome and cirrhosis.

Thesis No.: 13 Analysis of Single Trial Evoked Potentials Using Neural Network Structures and Radial Basis Functions.

Name: R. Murat Demirer, Year: 2002

Advisor(s): Halil Özcan Gülçür

Abstract: The single-trial evoked or event related brain potential (s-EP) estimation remains to be a very difficult problem due to many interfering noise sources and artifacts with spatio-temporally overlapping response components and due to the nonstationarity nature of these signals. In this thesis work a new class of neural network model and associated learning algorithm has been developed for s- EP estimation. The model is called M-NARMAX and uses a mixture of such techniques as radial basis functions (RBF), nonlinear auto regressive moving average modeling (NARMAX), neural networks, automatic order determination and maximum likelihood adaptive neural systems (MLANS). The use of radial basis functions and nonlinear auto-regressive moving average methods in the background make this estimation process very effective. The success of the model has been demonstrated in experimental studies with both synthetic and real data. The s-EP estimation technique developed has also been used in topographic dipole source localization. In order to reduce the dimensionality of the problem, a spatio-temporal transformation has been used, treating the human head as a spherical structure. Preliminary studies have shown that the accuracy of dipole localization is around 20-30 mm, throughout the latency period from 20 to 90 ms. The multi-channel M-NARMAX model considerably improves the quality of the estimates of single trial evoked potentials and makes them more functional and utilizable for both clinical practice and for research work. It also appears to resolve some of the previously unseen aspects of event-related signals. By combining the insights gained through detailed examinations of s-EPs using the techniques discussed here, with the available neurophysiological, neurometabolic, and neuroanatomical information a better understanding of mass neural processes of human cognition may be reached. This will allow more detailed study of changes in cognitive dynamics in brain-damaged persons, especially those with Alzheimer's or Parkinson's diseases.

Thesis No.: 12 A Model of Active and Attentive Vision.

Name: Çağatay Soyer, Year: 2002

Advisor(s): Işıl Bozma/Yorgo İstefanapulos

Abstract: Biological vision systems explore their environment by allocating their resources to interesting parts of a scene, using both physical and mental attention mechanisms. The result of this active and attentive vision behavior is a sequence of images obtained from different spatial locations at different times. However, temporal processes and integration mechanisms in the brain enable us to interpret this information and perceive a stable image of the environment. While models of such attention and perception mechanisms are invaluable to understand human vision, they are also increasingly used and improved by robotics and artificial intelligence researchers to achieve human- like performance. In a similar attempt, we propose a new and complete model of active vision behavior, based on confirmed biological evidence where available. The model consists of an attention system, temporal image sequence processing algorithms and an integrative visual memory. All components of the model are implemented on our mobile robot APES. Gaze control, sequence based scene recognition and visual integration tasks are assumed during experiments. Results of gaze control experiments clearly demonstrate a human-like selective attention behavior, which can be fully controlled by a number of parameters. In recognition and integration tasks, simple and complex scenes were successfully modeled and classified. Furthermore, our work on attentional image sequences raised a number of interesting questions, some of which have been answered in this thesis.

Thesis No.: 11 Comparative Analyses of Artificial Kidney Membranes and Influences of in Vivo Utilization on Their Properties and Performances in Terms of the Quality of the Materials and Hemodialysis Treatment.

Name: Buruk Armağan Konduk, Year: 2002

Advisor(s): Hikmet Üçışık

Abstract: The objective of this study was to identify factors affecting adequacy of haemodialysis and relations between them using Taguchi Method (fractional factorial experiments) throughout minimum of tests. Dialysis age, dialyzer membrane material, haematocrit, interdialytic weight difference, dialysate, pump speed, heparin type, and socio-economical status were applied as parameters for Taguchi Method in order to drive out not only their individual effectiveness on the therapy but also interactions among them. Adequacy of a hemodialysis treatment was decided according to Kt/V using Daugirdas-2 formula. Delivery of Kt/V of 1.2 was accepted as target value. Performing Analysis of Variance (ANOVA), dialyzer, haematocrit, pump speed and socio-economical status were found to have direct influence on the treatment quality, while dialyzer-interdialytic weight difference, dialyzer-haematocrit, dialyzer-pump speed, dialyzer-socio- economical status relations were detected as effective.

Thesis No.: 10 Novel Methods to Improve Acquisition of Transient Evoked Otoacoustic Emissions for Hearing Screening.

Name: Reis Burak Arslan, Year: 2000

Advisor(s): Yekta ülgen

Abstract: In this study, new signal processing methods are developed to solve some of the common problems in transient evoked otoacoustic emission (TEOAE) acquisition. The aim is to facilitate the universal auditory screening of newborns using TEOAEs. For this purpose, averaged and single sweep raw data were recorded using two different instrumentations. Various techniques used in digital signal processing of data have been applied for the first time, to the acquired TEOAE signal, and they are shown to yield satisfactory results in dealing with recording problems such as stimulus artifact, test duration, and noise reduction. In the first phase of the study, data are collected from normal hearing subjects, from different age groups, using the conventional data acquisition system in the clinic of the Marmara University Audiology department. Normal features of the TEOAE signal among age groups are statistically analyzed, then compared with time varying spectra obtained from parametric analysis. The following studies used the single sweep data collected in the Neurosensory laboratory of Biomedical Engineering Department at the University of Miami, from normal hearing young subjects. Initially, signal and noise characteristics under different recording conditions are determined and two Signal-to-Noise Ratio (SNR) based averaging methods are proposed accordingly. The first algorithm rejects the single sweeps whose power exceed a predetermined level, and yields better SNR at continuous noise. The second method is a selective averaging algorithm that sorts the single sweeps according to their noise powers and averages only the optimum number of sweeps. It is shown to be effective in reducing the total test time. In the next stage, two adaptive methods are implemented to enhance the signal to noise ratio of the response. Adaptive noise cancellation works for noisy environments while the adaptive signal enhancement improves the SNR of the emission at low stimulus levels. Otoacoustic emissions are known to be suppressed by noise masking. A novel approach, based on ipsilateral suppression of the emission, is shown to be successful in reducing the stimulus artifact. The benefits of simultaneously using the auditory brainstem response (ABR) and TEOAE testing in studying the suppression and reducing test time are also shown. All these methods, besides being effective in resolving the screening problems, also provided tools for the assessment of hearing status and investigation of the mechanics of the auditory organ.

Thesis No.: 9 Contribution of Superficial Layer Neurons to Presaccadic Bursts in the Superior Colliculus: A Whole-Cell Patch-Clamp Study in Brain Slices.

Name: Gülden Özen, Year: 1999

Advisor(s): Yusu p. Tan/George J. Augustine

Abstract: Brief electrical stimulation of the superficial layer of the superior colliculus in the tree shrew (Tupaia glass) evokes prolonged bursts of excitatory postsynaptic currents (EPSCs) in premotor cells of the subjacent intermediate layer. The large amplitude and long duration of these EPSC bursts suggest that intracollicular circuitry may contribute to the generation of the bursts of action potentials that premotor cells use to command saccades. In this study, we use whole-cell patch-clamp methods to examine the contribution of one component of this circuitry, the superficial layer, to the generation of EPSC bursts. Applying single, brief stimuli to the superficial layer of rat collicular slices evoked prolonged EPSC bursts that were similar to those previously described in the tree shrew. These EPSCs were sufficient to elicit bursts of action potentials that lasted as 300 milliseconds. To examine the contribution of neurons within the superficial layer to production of the EPSC bursts, we determined how these neurons responded to the same stimuli that evoked the bursts. Recordings from 61 superficial layer cells revealed 19 neurons that produced multiple action potentials following stimulation. Nine of these 19 neurons were types that project to the intermediate layer and, thus, could contribute to producing the EPSC bursts. The remaining cells did not generate trains of action potentials. Our results indicate that most superficial cells do not directly contribute to production of the EPSC bursts, but that a small number does have the properties necessary to provide this prolonged excitatory drive to the premotor neurons.

Thesis No.: 8 Evaluation of Altitude Decompression Procedures and Development of New Decompession Strategies.

Name: S. Murat Egi, Year: 1999

Advisor(s): Yusuf P. Tan/Yekta Ülgen

Abstract: Diving at altitude requires different tables than at sea level due to the reduction in surface level ambient pressure. In this work, the rationale for the algorithms extrapolating the sea level diving data are reviewed. When applied to different sets of maximum permissible tissue tensions (M value), the conservatism of an algorithm becomes a function of bottom time, depth and altitude. Aviation altitude exposure decompression sickness (DCS) data is also addressed. Animal experiments performed within the scope of this thesis proved that precordial bubbles can form during the ascent from sea level to 2000-m. supporting a far lower threshold for altitude DCS then the model outputs. Following three pioneering altitude diving expeditions to 2200, 3412 and 3980-m, a set of no- decompression stop (no-d) limits for 3500 m was calculated using linear extrapolation of US Navy M values decreased by 4 feet of sea water. This is a new method of altitude adaptation (NLHE, Nonlinear Hypobaric Extrapolation). These limits were tested at 3412-m. by 10 man/dive per profile without any case of DCS. 212 dives were achieved with a total bottom time of 4110 min. The mean DCS risk estimated according to precordial bubble scores (Spencer's Scale) ranges from 0.3% to 2.8% per profile. The last part of the thesis is devoted to the computation of decompression tables for 3500-m altitudes. This work suggests the use of a continuous variable for the compartment time constants, allowing the simulation of infinite number of compartments and reducing the discrepancy between different algorithms to a single M value expression.

Thesis No.: 7 Characterization of Processed Tooth Hydroxyapatite and Bioglass for Potential Applications in Dentistry

Name: Faik Nüzhet Oktar, Year: 1999

Advisor(s): Sabri Altuntaş

Abstract: In this study possible applications of bioceramics like hydroxyapatite (HA) and bioglass in dentistry have been studied. HA was derived from freshly extracted human teeth in laboratory conditions as plasma coating and grafting material and basic techniques for material characterization were performed. The HA produced by this method is simple and economical when compared with conventional methods which are tedious and time consuming. Bioglass compositions used in this study, were produced from reagent grade fine chemicals and some porous structures were prepared. Implant prototypes prepared from titanium rods, were coated with HA powder using a plasma coating unit. The HA produced by this method has been demonstrated to have the potential to become a superior graft material in veterinary orthopedics. Plasma spraying studies agreed with the results in the literature. Pathological results of the animal studies have been affirmative. For animals nuclear bone scintigraphy studies were performed to follow the sseointegration process in HA/ bioglass grafting cases. It was observed that bone scintigraphy was a valuable method to follow the metabolic activity of bone cells when compared with planar X-ray films. Graft studies were also performed using plaster of Paris which is another bioceramic. An active drug delivery system was evaluated based on its rapid solubility characteristics. Pathological results and high performance liquid chromatography results indicated that this material has potential as a drug delivery system.

Thesis No.: 6 The Mechanical and Biological performance of the Alternating sliding knots with different patterns in Abdominal would closure.

Name: Zeina Babetty, Year: 1998

Advisor(s): Sabri Altuntaş

Abstract: New knot configurations, consisting of alternating strands with different patterns, have been studied from mechanical and biological perspectives in order to determine whether they would be suitable for abdominal surgery, as compared with conventional sliding knots. Mechanical properties of these new knots were compared with those of the classical sliding knots and single threads for silk and nylon sutures under dry conditions. From the mechanical perspective, the new knots showed better knot holding capacity and efficiency. In the in vivo implantation tests performed on the rat abdominal wall, the alternating sliding knots with different patterns were found to be more efficient and secure than the classical sliding knots. The knot configuration, postoperative period, suture material and size were important factors in determining the knot holding capacity. From the biological perspective, these new knots provoked tissue reaction similar to the classical sliding knots. Because nylon is less pliable than silk, its use resulted in higher effective knot volumes, causing more pronounced tissue reaction. To test the bacterial adherence to the knots, in vitro and in vivo tests were performed in rats. The degree of the elicited infection correlated well with the capability of bacteria to bind to the suture. It was observed that the knot configurations and the suture sizes did not have much effect on bacterial adherence. Due to the presence of interstices between throws, the knots had greater capacity to retain bacteria than the single threads for both silk and nylon, thus promoting infection. The elasticity and stress-relaxation properties of these knots were compared to those of single threads of silk and nylon. The elasticity of the knots, in general, was higher than that of the threads for both materials. The silk showed decreased elasticity at high extension levels, while nylon showed increased elasticity. In stress relaxation tests, the residual load fraction of the knots was found to be higher than that of the threads at all extension levels. A model was created to study the effect of several factors on the suture pullout force in the abdominal wall. Incisional direction, knot configuration, strain rate and tissue healing strength were important factors in determining the suture pullout force. In conclusion, we do recommend the use of the alternating sliding knots with different patterns in abdominal surgery instead of the currently used sliding knots.

Thesis No.: 5 Classification, Visualization and Transient Analysis of Respiratory Sound Patterns

Name: Emin Çağatay Güler, Year: 1998

Advisor(s): Yasemin P. Kahya/Bülent Sankur

Abstract: Among the methods for the diagnosis of respiratory disorders auscultation is still the most rewarding method since it is simple, patient-friendly and non-invasive. Recent advancements in measurement and signal processing techniques have opened the path for intelligent stethoscopes. By an intelligent stethoscope, one intends a computerized auscultation device which can register and process the sound signals, display them with sophisticated visualization techniques and can provide to the physician diagnostic aids. This research is a case in point that it advances and investigates various signal processing and classification techniques for an intelligent stethoscope. Firstly, for diagnostic purposes, a multi-stage signal classification and decision fusion scheme has been developed. This scheme significantly improved the classification performance by having on one hand two-tiered decision mechanism rather than a single stage classification and on the other hand by combating the non-stationarity of respiratory sounds due to their cyclic behavior. Secondly, a nonlinear mapping method for the interactive analyses of sound patterns has been developed. Experiments in visual assessment of respiratory sound patterns using were promising from the medical diagnostic point of view both due to its flexibility and the fact that it outperformed competitor mapping techniques in the literature. Thirdly, a transient detection scheme based on the use of time-scale analysis and nonlinear operators has been investigated. The method was found to be superior to existing algorithms in both detection performance and fidelity of extracted waveforms. In conclusion, these three advances in respiratory sound analysis and classification contributed to the development of an auscultation based diagnostic device implementable on any signal processing board on PC.

Thesis No.: 4 Cardiopal: Cardiac Passive Acoustic Localization and Mapping Using 2-D Recordings of Heart Sounds

Name: Yıldırım Bahadırlar, Year: 1997

Advisor(s): Halil Özcan Gülçür

Abstract: A non-invasive method is proposed for acoustical detection of coronary artery disease in a normal hospital environment. The diastolic heart sounds recorded via a high sensitive phonocardiography system are utilized to differentiate the coronary artery victims. A frequency- domain adaptive filter is used to effectively eliminate the background noise from these weak signals and to promote Autoregressive (AR) parameters having distinctive features between normal and diseased subjects. For the noise cancellation process an auxiliary sound channel is also included in the recording system. Clinically valuable correct classification rates are reached by using the AR parameters as feature vector for two objective classifiers, namely a two-layer perceptron and the K- means classifier. The second heart sounds are decomposed into damping sinusoids by using forward prediction, and a correlation between the systolic blood pressure in the aortic root and parameters of the damping sinusoids is investigated. The damping parameter with its intrinsic immunity reveals the highest and statistically significant correlation with the systolic pressure. This new approach is proposed for continuous pressure measurement, but it needs extensive clinical investigations. A microphone array system and an array signal processing method is developed to localize hypothetical sound sources in the heart of the adult and the fetus. This approach is totally original in the field of digital phonocardiography. 2-D and 3-D images of the sound sources are estimated by means of a signal propagation model and a subspace-based array processing algorithm (MUSIC).

Thesis No.: 3 Analysis of Averaged and Single Evoked Potentials Using Damped Sinusoids and Wavelet Basis Functions

Name: Ahmet Ademoğlu, Year: 1995

Advisor(s): Yorgo İstefanopulos/Halil Özcan Gülçür

Abstract: Two new modeling techniques, based on the damped sinusoids and the wavelet basis functions, are proposed for the analysis and investigation of Evoked Potentials (EP). The damped sinusoid modeling is applied to the averaged and the single trial EPs and the relation between the spontaneous brain electroencephalogram (EEG) and EP is observed as a phase reordering and amplitude enhancement of certain damped oscillations. The method which estimates the single trial EP in EEG, allows for tracing the single trial variabilities of the EPs during a recording session. The wavelet transform is applied to the averaged and single trial EPs for the time-frequency analysis of the oscillations occurring in different frequency bands of spontaneous EEG. The relation between EEG and EP activity is observed as an amplitude enhancement and a phase alignment of otherwise randomly phased oscillations in the spontaneous EEG. A selective averaging method is proposed based on these findings. The wavelet transform is applied to the averaged pattern reversal visual EPs collected from normal and Alzheimer's diseased subjects. A consistent differentiation of phase behavior in slow oscillations in the delta-theta band (0-7 Hz) is observed between the normal and pathological waveforms.

Thesis No.: 2 pH Dependence of Histamine Modulation on NMDA Response in Hippocampal Slices

Name: Hale Saybaşılı, Year: 1995

Advisor(s): Yusuf Tan /Helmut L. Haas

Abstract: The histaminergic system in the brain emanates from the tuberomammilary nucleus of the posterior hypothalamus and projects to the whole central nervous system. In this research, the effect of histamine was investigated in the CA1 region of the hippocampus of rats in vitro. The enhancement of activity mediated by classical histamine receptors has been confirmed and a new independent action of histamine on N-Methyl D-Aspartatic acid (NMDA) receptors has been described in, 1. hippocampal slices as an epileptiform field activity in magnesium free medium, representing NMDA receptor mediated extracellular activity ,2. thin hippocampal slices with patch-clamp technique as an effect on the NMDA components of excitatory postsynaptic currents. The extracellular activity evoked by the stimulation of Schaffer collateral-commissural pathway was recorded from CA1 stratum pyramidale and stratum radiatum The NMDA components of excitatory currents evoked by glutamate in the CA1 region of rat hippocampal slices and their modification by histamine were investigated by using the patch-clamp tight seal whole cell recording technique. In this study it has been found that histamine has no influence on non-NMDA current but effects the NMDA current in a pH dependent way. Histamine potentiates the NMDA current at pH 7.2 while it depresses the current at pH 7.6. The NMDA current modification by histamine was not mediated by the activation of known histamine receptors of H1, H2 or H3 type. The effect resembles the known interaction of polyamines with the NMDA receptor-ionophore complex. This work is consistent with the concentration clamp experiments in isolated hippocampal pyramidal cells and emphasizes the physiological and pathophysiological implications: Slight shifts in pH as shown here to profoundly influence the histamine action occur locally during intense nervous activity, tetanic stimulation and globally during anoxia. The modulating action of the histaminergic system in the brain will be specifically targeted towards plasticity under these conditions.

Thesis No.: 1 A Computerized Pulmonary Diagnosis System.

Name: Yasemin Palanduz Kahya, Year: 1987

Advisor(s): Yusuf Tan/Ömer Cerid

Abstract: The lung, the ventilatory apparatus, has the task of producing an alternating mass flow of gas between the external atmosphere and the lung alveoli, during which it functions both as a mechanical pump and as a gas exchanger. Spirometry is a method which aids in the diagnosis of the condition of the lung as a mechanical pump through pulmonary function tests. In this work, a microprocessor-based system has been developed to improve on the accuracy of the measurement of the pulmonary function tests and at the same time to reduce the time required for analysis of the respiratory data. However, as such an approach by itself does not evaluate the gas exchanging function of the lung, in addition to spirometry, the system designed to incorporate monitoring the partial pressure of inspired and expired oxygen via two additional parameters, defined in this work, to give the user an insight into the condition of the lung as a gas exchanger. These parameters are calculated from measured quantities and are compared with values calculated from a lung model. The simultaneous measurement of the flow data and oxygen partial pressure offers the physician a more complete perception of the state of the lung, through more accurate evaluation of various respiratory parameters. The design replaces in many aspects more costly and multi-instrument systems with one system which is easily operated and requires minimum user intervention. The system calibrates itself before each test and offers the user the option of selecting among three tests. The system, furthermore, is interactive via a visual display, and a hard copy of the results and graphs can be obtained upon user command from the printer. The system is especially useful in mass screening where optimization of time and costs is required. Finally, both the hardware and software are flexibly designed to permit future expansion.