Amplification of Glioma Radiation Therapy through Iron Oxide Nanoparticles

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This research aims to examine the effect of therapeutic gamma radiation in the presence of iron oxide nanoparticles (NPs), specifically for applications to glioblastoma multiforme (GBM) brain cancer. Standard treatment for GBM currently consists of intensive surgery and aggressive radiation therapy. Due to the sensitive locations of the tumors in the brain, these treatments can cause negative side effects without significantly improving survival rates. Biocompatible iron oxide NPs have been developed for their novel tumor-targeting capabilities, allowing for precise drug delivery, minimizing negative side effects to healthy tissue. It has been theorized that NPs could also amplify effects of radiation within tumor cells while reducing radiation effects in surrounding healthy tissue. To this end I aim to evaluate multiple distinct NP formulations to optimize the amplification of reactive oxygen species (ROS), and subsequent DNA damage during radiotherapy. Initially, various concentrations of each NP and a range of radiation dosage are tested to enhance ROS production. In vivo testing through mouse survival studies has been successful. Currently, further in vitro studies assessing ROS production, DNA damage, and cell survival are being conducted to accumulate further evidence in support of the NP’s ability to efficiently and successfully enhance drug treatment of GBMs.

An Acoustic Beacon for Facilitation of EEG Monitoring of Deep Brain Activity

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Electrophysiological modalities facilitating the noninvasive monitoring of brain function, including those associated with neurological disorders such as epilepsy, are currently restricted to superficial brain structures and have limited anatomical specificity. Previous work demonstrated that transcranially applied, pulsed focused ultrasound (pFU) could non-invasively activate neural circuits within brain at frequencies associated with endogenous brain activity (below 100 Hz). With this as motivation, we hypothesized that pFU could ‘tag’ endogenous brain activity within the small volume of deep brain tissue at its focus with a unique, non-endogenous signature nonetheless detectable by standard electrophysiological means. As a first step towards a full test of this hypothesis, we sought here to demonstrate generation of that unique electrophysiological signal, in vivo. Specifically, we performed an experiment on anesthetized rats, delivering transcranial pFU in pulses 1050 times per second to rat brain in an alternating on/off scheme while recording brain activity through use of a subdermal electroencephalogram (EEG) needle electrode montage. We demonstrated in vivo the presence of a statistically significant 1050 Hz electrophysiological signal only when the animal was alive and ultrasound was on. Also, we observed directly measured event-related 3-40Hz EEG signals over time in a subset of our data commensurate with beta and gamma activity inferred from demodulation amplitude analysis of our pFU-induced 1050 Hz signal. Current work is aimed at finding protocols that minimize the change to endogenous activity as well as the demodulated low frequency signals while administering the acoustic beacon in a robust manner. Demonstration of a unique and detectable electrophysiological signal gener-
Development of an Implantable Electromagnetic Field-Emitting Device for Cancer Treatment

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Low intensity non-thermal non-ionizing electromagnetic fields (EMF) in the ranges of extremely-low to low frequency (< 200 kHz) have been shown to kill cancer cells in various studies. It is difficult to concentrate external electromagnetic field in tumor site to enable effective cancer treatment. We are studying EMF-emitting microchips that are small in size and can be easily surgically implanted into a tumor. The microchip emits electromagnetic fields when it is activated by an ‘activator’ outside of the body. Since the chip is in close proximity to cancer cells within the tumor, cancer cells would be exposed to a high local field that kills the cells. A prototype of microchip (cylindrical, ~12 mm in length, ~2 mm in diameter) will be tested on human leukemia, breast cancer, and liver cancer cells in vitro. Cancer cells will be incubated for 24 hours at 37°C in a humid atmosphere of 5% CO₂ and 95% air. Four identical flasks of cells will be prepared. After initial count, a microchip will be placed in two of the flasks. Two flasks (one containing a microchip and other not) will be exposed using an activator. The other two (with and without microchip) will be sham exposed, i.e., they will be subjected to the same experimental procedures as the ‘exposed’ samples except that the activator will not be turned on. During exposure, cells will be maintained in a water bath at 37°C. Viable cell count will be performed at 24 hours after exposure. Our preliminary results are encouraging. We have found that EMF emitted from microchips could effectively kill human leukemia and breast cancer cells. From in vitro data, we anticipate to proceed to in vivo studies.

NAIL: Nucleic Acid Detection Using Isotachophoresis and Loop-Mediated Isothermal Amplification

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The recent Ebola outbreak has demonstrated the need for rapid and accurate diagnostics tests for infectious diseases to improve global health. Nucleic acid amplification tests are the gold standard for many infectious disease diagnoses due to high sensitivity and specificity, rapid operation, and low limits of detection. Despite the advantages of nucleic acid amplification tests, they currently offer limited point-of-care (POC) utility due to the need for sophisticated instruments and laborious sample preparation. We have developed a point-of-care Nucleic Acid Isotachophoresis LAMP (NAIL) diagnostic device. NAIL uses isotachophoresis (ITP) and loop-mediated isothermal amplification (LAMP) to extract and amplify nucleic acids from complex matrices for point-of-care applications. ITP is an electrokinetic separation technique that uses an electric field and two buffers to extract and purify nucleic acids in a single step with minimal sample preparation. LAMP amplifies nucleic acids at constant temperature and produces large amounts of DNA that can be detected using a mobile phone camera. The device requires minimal user intervention because capillary valves and heated air chambers act as passive valves and pumps for automated fluid actuation. NAIL has been shown to extract and detect pathogenic E. coli O157:H7 cells from whole milk samples. The NAIL device has a limit of detection of 1,000 CFU/mL for E. coli cells artificially inoculated into whole milk, which is two orders of magnitude improvement to standard in-tube LAMP reactions with diluted milk samples and comparable to lab-based PCR systems. The NAIL device potentially offers significant reductions in the complexity and cost of traditional nucleic acid diagnostics for point-of-care applications.

Effect of Stone Characteristics on Fragmentation of Kidney Stones Treated with Burst Wave Lithotripsy

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Burst wave lithotripsy (BWL) is an experimental treatment for kidney stones, using ultrasound pulses to extracorporeally break stones into small, passable fragments. BWL has pressure amplitudes significantly lower than those used in shock wave lithotripsy (the most common kidney stone treatment in the U.S.), potentially minimizing injury to surrounding tissue. This study aimed to determine the effect of stone dimensions and hardness on fragmentation of stones treated with BWL. Cylindrical stone models of variable length (8-26 mm, 6 mm diameter), and diameter (4-14 mm, 10 mm length) were cast using two different plasters: BegoStone (Bego), which mimics hard stones, and Ultracal-30 gypsum (U30), which mimics soft stones. Stones were treated for 10 minutes using a 170 kHz focused ultrasound transducer. After exposure, stone fragments were weighed to determine the fraction broken and fragment size distribution by weight. Both types of stone models experienced fracturing and fragmentation when exposed to BWL, though U30 stones fragmented more. Smaller diameter stones tended to have the highest percent-by-mass fragmentation. For Bego stones, the smallest diameter had 75% fragmentation, whereas the largest had...
only 5%. U30 stones of variable diameter showed a similar trend, from 98% fragmentation in the smallest diameter to 52% in the largest. Most fragments from both types of stones were clinically passable (<4 mm). Length seemed to have less impact on fragmentation than diameter, as most length stones of both types had greater than 70% fragmentation by mass. Longer stones tended to produce fragments that would not be clinically passable, but this was likely due to the experimental setup rather than the treatment. While BWL can break both hard and soft stones, this study provides useful data to account for stone size and composition during treatment planning, so that stones can be reduced to small, passable fragments.

**Ultrasound Methods for Improving Sizing Accuracy of Kidney Stones**  
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Although Ultrasound (US) provides an inexpensive, minimally invasive, radiation free method for the sizing of kidney stones, it is known to overestimate stone size so I explored using the acoustic shadow produced behind kidney stones as a possible form of more accurate sizing. Forty-three human kidney stones were used for this study and each stone was imaged with a software based US system at three different depths and with three different imaging modalities. These stone images were reviewed by four separate operators, all of whom were not told the true measurements of each stone. Each operator measured both the stone width and the width of the acoustic shadow behind the stone. The error in stone size was then calculated as the measured width minus the true width. The average error in stone size when the stone image was captured with the conventional B-mode modality was 1.4 ± 0.8 mm. The average error for spatial imaging was 1.6 ± 0.8 mm while for harmonic imaging the average error was 0.7 ± 0.8 mm. In comparison, the average error in stone measurement when the acoustic shadow width was measured was 0.2 ± 0.7 mm, 0.4 ± 0.8 mm, and -0.1 ± 0.9 mm, respectively. The error in measurement of stones increased with depth when the measurements were based on the stone image but not when based on the shadow. Through the use of this in vitro model, a method was developed to reduce stone overestimation to 1 mm. This method uses the stone’s acoustic shadow width as a source of size indication as well as harmonic imaging. By measuring the width of the acoustic shadows, a significant improvement of sizing accuracy was observed in comparison to the traditional method of measuring the stone width using conventional B-mode imaging.

**An Open-Sourced Silicon Photonic Biosensor Characterization Platform for Rapid and Affordable Label-Free Biosensing**  
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The Enzyme-Linked Immunosorbent Assay (ELISA) represents the current gold standard for the clinical diagnostic, but it requires complex labeling and amplification to quantify specific biomolecular targets. As a result, the ELISA is time consuming and costly. Thus a faster, simpler, and lower-cost alternative is in demand. My project aims to develop a rapid and affordable diagnostic biosensor platform that can be administered in the Point-Of-Care setting. In our silicon photonic sensor chip, we exploit a unique feature of light when it is confined within a silicon waveguide with dimensions comparable to its own wavelength. A portion of the light’s energy is located outside the waveguide, known as an evanescent field, and is capable of sensing molecules that bind on the sensor surface. While the design and fabrication of these sensors can be readily accomplished, device characterization and analysis remains challenging due to the precision required to optically test submicron-scale components. To address this need, we have customized a low-cost test bench to perform sensor characterization and further biosensor experiments on silicon photonic biosensors. Towards this end I have designed the test bench software, which employs an industrial standard Model-View-Controller architecture, for instruments integration and experiments orchestration as well as data acquisition and analysis. I have also placed significant effort in simplifying the platform chip-scale integration of otherwise complex instrumentation. With this platform, I have characterized multiple sensors through salt step experiments (i.e. NaCl solution with various concentrations), acquisition and analysis of optical power spectrum data, mathematical modeling and estimation of key parameters. Characterization results showed an improved sensing capability, compared to currently available photonic sensors in the market, which we have validated using a modified sandwich immunosassay. Our results show significant promises for our design as a diagnostic biosensor platform which will expand the capabilities of silicon photonic-based sensing platforms.