UNIVERSITY of WASHINGTON

Undergraduate Research Symposium May 17, 2013 Mary Gates Hall

Online Proceedings

POSTER SESSION 1

Commons East, Easel 72

11:00 AM to 12:30 PM

Acoustic Evaluation of Hepatic Steatosis

Ameen Tabatabai, Sophomore, Bioengineering
Mentor: Wayne Kreider, Applied Physics Laboratory
Mentor: Yak-Nam Wang, APL
Mentor: Michael Bailey, APL
Mentor: Adam Maxwell, Urology

Liver transplantation is a widely performed treatment for patients with end stage liver disease. Each day, the liver transplant waiting list grows longer due to a shortage of acceptable organs. Hepatic steatosis in donor livers is an increasing problem that contributes to discarding otherwise-transplantable livers. Numerous studies and surgeries have shown that high fat content in livers correlates with poor graft function and lower patient survival. Longer waiting lists are causing transplant centers to consider moderately steatotic livers as a part of extended donor criteria. However, a method is needed to objectively quantify fat content in livers in order to select suitable organs. Many studies over the past 30 years have characterized a correlation between fat content of livers and acoustic properties such as sound speed and attenuation. This research seeks to employ an acoustic caliper device to acquire acoustic measurements that can be used to quickly, accurately, and noninvasively evaluate the fat in transplant donor livers. Sound speed and attenuation were measured by transmitting short pulses of ultrasound at frequencies from 1-10 MHz through excised pig and cow livers. Liver thicknesses were measured with a dial caliper to permit sound speed estimates, and reference measurements were taken in water to calculate the additional attenuation created by the presence of the liver. In addition, a thermocouple was used to take precise temperature measurements in liver and water, since sound speed varies with temperature. Although fat content was not quantified, sound speed and attenuation did correlate with the presence of visually observable fat. However, significant variabilities between measurements were also found with regard to the preparation of the liver samples and tissue inhomogeneities. This work has led to ideas for an improved acoustic caliper device and for testing lipid emulsions as tissue phantoms for evaluating measurement capabilities.

POSTER SESSION 4

MGH 241, Easel 157

4:15 PM to 5:45 PM

Characterization of Novel Chemical Inhibitors for the Plasma Membrane Monoamine Transporter and Organic Cation Transporter 3

Ji Soo Kim, Senior, Bioengineering, Biochemistry
Mentor: Joanne Wang, Pharmaceutics
Mentor: Haichuan Duan, Pharmaceutics

Deficiencies of monoamine neurotransmitters including serotonin, norepinephrine, and/or dopamine have been associated with many CNS diseases including depression, schizophrenia, ADHD, autism, Parkinson's disease, and Tourette syndrome. The intensity and duration of monoamine signaling is mainly determined by the clearance of the released transmitters through uptake1 and uptake2 transporters. The recently discovered uptake2 transporters including the plasma membrane monoamine transporter (PMAT) and organic cation tansporter3 (OCT3) have been less studied partly due to the lack of specific inhibitors. Recently, inhibition of PMAT and/or OCT3 has been proposed as a strategy for the development of antidepressant drugs with improved efficacy and faster onset of actions. The goal of this project is to characterize specific chemical inhibitors for PMAT and OCT3. Previously, 10-40 small molecule inhibitors for PMAT and OCT3 were identified from high throughput screening. We will choose two to three inhibitors for PMAT and OCT3 obtained from the initial screen and further analyze their potency, specificity and mechanism of inhibition towards PMAT and OCT3. We first will determine their inhibition potencies (IC50) towards PMAT and OCT3 using radiotracer uptake assays in cell lines stably expressing these transporters. Preliminary data showed that two compounds inhibited OCT3 with IC50 values of 1.97 ± 0.766 and 2.86 ± 0.532 μM. One compound inhibited PMAT with an IC50 value of 2.15 ± 0.537 μM. Further studies will be performed to determine the specificity and mechanism of inhibition for these inhibitors. The proposed studies may lead to novel, highly specific and potent PMAT and OCT3 inhibitors that could be further evaluated and developed in preclinical models for the treatment of depression and other monoamine-related diseases.

POSTER SESSION 4

MGH 241, Easel 138

4:15 PM to 5:45 PM

Utilizing Thermal Dose in Hyperthermia of Pancreatic Cancer Cells

Leslie Ann Cornaby, Senior, Bioengineering
Mentor: Joo Ha Hwang, Medicine
Mentor: Yak-Nam Wang, APL
Mentor: Navid Farr, Bioengineering

Pancreatic cancer is the fourth most common cause of cancer-related deaths in the United States. The overall survival rate is low because current therapies are ineffective. However there is growing research that High-Intensity Focused Ultrasound (HIFU) can be used to significantly improve current therapies for treating pancreatic cancer. HIFU works by accumulating ultrasound waves (i.e. energy), which generates heat causing tissue damage (i.e. hyperthermia). The thermal damage caused is measured by using thermal dose. Thermal dose describes the temperature the tissue is treated at and how long that treatment occurs. The theory of thermal dose has been tied to hyperthermia of cancer cells since at least the 1980s and there is a lot of strong mathematical background behind the time-temperature relationship. However with the rapid development of clinical hyperthermia for cancer therapy there is a need for accuracy when it comes to predicting thermal dose. My research focuses on whether or not equivalent thermal doses actually mean equivalent cell death (with cell types Panc-1 and MIA PaCa) and if this can be translated into a clinical setting where higher acoustic power can be used (i.e. using higher energy with HIFU to get lower time of treatment). I simulate HIFU by treating pancreatic cancer cells in water baths at equivalent thermal doses and measure cell survival with spectroscopy. My initial results suggest that the thermal dose relationship is accurate in relating amounts of cell death. An early conclusion from this is that thermal dose can be used to provide better calculations in a clinical setting and help evaluate data. Patients may even be able to experience shorter treatment times through using higher acoustic power with HIFU resulting in a more comfortable experience.

POSTER SESSION 4

MGH 241, Easel 142

4:15 PM to 5:45 PM

Comparative Cytotoxicity Study of Chemotherapeutic Agents on Pancreatic Cancer Cell Lines

Sarah Haejin (Sarah) Kang, Sophomore, Pre-Health Sciences
Ann Booyo (Ann) Lee, Junior, Pre-Health Sciences
Mentor: Joo Ha Hwang, Medicine
Mentor: Yak-Nam Wang, APL

According to the American Cancer Society, pancreatic cancer has a five-year survival rate of less than 15 percent and is the fourth leading cause of death from cancer in the United States. Present-day chemotherapy treatments attempt to lengthen the lives of patients but are often unsuccessful due to the nature of the disease. Doxorubicin and Gemcitabine are already commonly prescribed as pancreatic cancer treatments while Thermodox®, a lysolipid thermally-sensitive liposome (LTSL) technology, is still undergoing clinical trials. LTSLs encapsulate Doxorubicin releasing the drug when the agent is exposed to temperatures greater than 40 degrees C. The goal of this study is to compare the in vitro cytotoxicity of four chemotherapeutic conditions: unheated Thermodox®, heated Thermodox®, Doxorubicin, and Gemcitabine. Varying concentrations of each drug condition are applied to LMP, PANC-1, and Mia-PaCa cell lines, which originate from mouse and human pancreas carcinoma. The remaining post-treatment viable cells and relevent controls are then stained with a fluorescent dye (Hoechst 33342) and analyzed by a fluorescent plate reader, from which cell death can be determined. Preliminary results show that that unheated Thermodox is not toxic to cells, and heated Thermodox®, Doxorubicin, and Gemcitabine is toxic to cells. The results of this experiment can lead to greater knowledge of the cytotoxicity of current chemotherapy agents as well as new technologies in cancer treatment.