REU Project Descriptions

BME Summer Internship Program
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Effect of Bisphosphonates on Bariatric Surgery-Associated Bone Loss in Older Adults with Obesity

Osteoporosis is a significant concern in older adults with obesity, which may be exacerbated by bariatric surgery due to the magnitude of weight lost and malabsorptive issues. Clinical guidelines support antiresorptive bisphosphonate medication use in bariatric surgery patients with osteoporosis, but no studies have examined the efficacy of oral bisphosphonates to prophylactically attenuate surgical weight loss associated bone loss. This 6-month randomized controlled trial of 24 older (50+ years) sleeve gastrectomy patients will examine the efficacy of bisphosphonate use (versus placebo) in the prevention of surgical weight loss associated bone loss.

The student will: 1) review the literature on bariatric surgery-associated bone loss and techniques for measuring bone health using computed tomography (CT), 2) form a hypothesis to test the effect of bisphosphonate use on a CT-derived bone outcome such as bone mineral density (BMD), cortical thickness, bone strength, or fracture risk measured from the hip and spine of bariatric surgery patients (Figure 1), and 3) experimentally test the hypothesis by applying learned CT analysis and finite element (FE) modeling techniques to collect, analyze, and draw conclusions from the resulting bone outcome data.

Location: Wake Forest Baptist Health

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Project 2

Surgical Robotics and Biomechanics

Advancements in robotics, computing power, medical imaging and processing, augmented reality, artificial intelligence, motion tracking, and topology scanning are combining to increase the performance and applications of robotic surgery. The trend is driving down system cost and improving effectiveness, and prevalence in care pathways. Biomedical Engineering is fostering opportunities for collaborative research and technology development with physicians and industry partners. We have interest to investigate the following areas of surgical robotics: surgeon to robot interface, force feedback control, autonomous operations, robot tool and tissue interaction, laparoscopic tissue mechanics, surgical instrument design, visualization aids, augmented reality interfaces, training tissue surrogate development, analysis of training and surgical operation, artificial intelligence surgical aids, patient safety, operating room safety & efficiency.

The student will research one or more of these areas by reviewing current understanding and technology development through literature review. This will be followed up by a proposal of novel technology development or pilot research and experimentation. This may including hypothesis formation, experimental design, cadaveric testing, and data analysis. The student will receive training in robot control and any other relevant technical skills. Outcomes from their summer research experience will contribute to proposals for grant funding.

Location: Wake Forest Baptist Health

Philip Brown, PhD

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Additive Manufacturing for Clinical Research

Additive manufacturing, also known as 3D printing, is quickly becoming a major player in medical device manufacturing and clinical care with major companies. The FDA is actively releasing regulation and guidance enabling the use of additive manufactured medical devices. Advances in this technology in the last several years have allowed for production of efficient, economic, bio-mimetic, and patient specific medical devices useful in all fields of medicine. Parts produced offer unique complex geometries and material properties only possible through this technology. The Wake Forest Biomedical Engineering Department is eager to invest and develop unique research opportunities in the field of clinical additive manufacturing and would like to support clinical department interested in this transformative technology.

The student will aid in research and operation of clinical and biomechanics 3D printing support. This will involve review of literature on current and future applications and techniques of clinical 3D printing. The student will receive training in operation of professional software and hardware tools for industry quality 3D printing systems. Mechanical material testing and analysis may also be conducted.

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Novel Research and Medical Device Development

There are several opportunities within Biomedical Engineering and through collaborations with orthopedics, neurosurgery, the center for biomedical imaging, plastic surgery, and others for the development of novel medical and research devices. These include experimental fixtures, exercise/rehabilitation machines and instruments, as well as surgical tools and hardware. Students selected for this project will be heavily engaged in the design process, conceptualization, prototyping, quality assurance, and experimental evaluation of multiple concurrent device development projects.

The student will aid in research and development of novel medical devices and operation of 3D printing support. This will involve review of literature on current and future medical procedures and techniques. The student will receive training in operation of professional software and hardware tools for industry quality CAD and FEA software as well as 3D printing systems. Mechanical material testing and analysis may also be conducted.

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Exploiting 3D Tissue Engineered Models to Study Blood Brain Barrier Dynamics and Repair During and After TBI

TBI often results in damage to the blood brain barrier (BBB), profound neuroinflammation, and dysregulation of metabolic processes. This project exploits a tissue engineered model of the BBB to elucidate mechanisms linking the initial biomechanical impact to altered inflammatory and metabolic processes. Experiments will characterize the inflammatory and metabolic changes following varying degrees of brain injury (by increasing severity and magnitude of tissue deformations) to identify key biological and molecular signatures associated with TBI and early stage recovery of TBI, by repairing the BBB.

The student will: 1) review literature on TBI and mechanisms, including the interplay between BBB damage, vascular permeability, and physical and chemical properties of the brain, 2) design a hypothesis-driven project to evaluate the efficacy of treatments to restore the blood brain barrier, promote neuronal repair, and provide necessary nutrients and oxygen to optimize tissue recovery, and 3) apply learned laboratory skills including cell- and tissue-culture, microscopy, biochemical assays, and image acquisition to gather and analyze experimental data to test the hypothesis and develop TBI treatment recommendations.

Location: Wake Forest Baptist Health

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Human Body Model Development for Trauma Research

Computational modeling is a growing component of injury biomechanics and trauma research. This project is a multi-center effort developing a next generation set of human body finite element (FE) models for enhanced injury prediction and prevention systems. The student will learn specific skills that are highly translatable to future graduate research experience including finite element volume meshing, high performance computing and morphometric operations such as scaling and medical image analysis. There will be a specific emphasis on applying the scientific process to these efforts. Students will review the literature in the subfield of modeling in which they are working. Computational efforts will focus on hypothesis driven activities, with simulations designed and conducted by the student to verify or refute their inquiries. These activities will be focused around model validation, studies related to injury risk predication in a given environment, or how best to scale results to match literature data from different body habitus.

This research effort will be in the Center for Injury Biomechanics (CIB) and you will have the opportunity to work on a range of projects in the field of automobile safety, military restraints, and sports biomechanics. The CIB has two primary research facilities. The first is in the WFU School of Medicine in Winston-Salem, NC and the second is at Virginia Tech. The research at the CIB combines experimental testing, computational modeling, and case analysis to investigate human injury biomechanics.

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An emerging area of interest is the study of bio-heat transfer for modeling brain therapeutics and pathology such as epilepsy. This project will focus on the study of heat transfer as it pertains to human body modeling, specifically quantifying thermal dose in the human body based on well-known bio-heat transfer experiments in the literature. The student will conduct experiments on a previously-developed brain phantom which simulates cooling therapy.

Next, using an established finite difference model, the student will calculate the predicted transient temperature response of both the phantom and of a brain, and compare those mathematical results to those from the lab experiment. In conjunction with this effort, the phantom will be improved upon in a laboratory setting in order to ensure repeatability of experiments as well as the ability to match the expected physiological response.

Lastly, the student will be tasked with developing prototypes of novel cooling devices within relevant design criteria. Understanding the context and application of such a device will be key to development.

**Location:** Wake Forest Baptist Health

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Underbody Blast Biomechanics

Underbody blast loading creates vertical accelerative loading and is a significant threat to the modern warfighter. The goal of this project is to develop a biomechanically based strategies for mitigating injury in these environments. This includes team oriented work on the development of anthropomorphic testing devices (ATD, aka dummy) with biofidelic capabilities specific to the underbody blast environment. Additionally, human body finite element modeling in this environment will be a component of the project. Human modeling work is focused on the hypothesis that computational human body models can be used this environment to predict injury and thus be used as a novel surrogate to establish preliminary guidelines on human tolerance to severe vertical loading. Component level tests will be evaluated for statistically significant agreement with experimental trials and we will explore the suitably of a modeling approach for foundational biomechanical work in vertical loading. The student will assist in the development and execution of code to generate human injury probability curves, and use of finite element models in matched trials of dummy and laboratory tests.

This research effort will be in the Center for Injury Biomechanics (CIB) and you will have the opportunity to work on a range of projects in the field of automobile safety, military restraints, and sports biomechanics. The research at the CIB combines experimental testing, computational modeling, and case analysis to investigate human injury biomechanics.

Location: Wake Forest Baptist Health

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Sensor technology offers researchers and consumers the ability to collect head impact data in the real-world; however, the accuracy of such sensors has been limited. This project involves development, testing, and field deployment of a novel instrumented mouthpiece in contact sports (e.g. football, soccer, hockey) and everyday activities (e.g. sitting, running).

The student will: 1) review literature on head kinematics in athletic and everyday activities, and 2) design a hypothesis-driven project to evaluate kinematic data collected from the mouthpiece. The student will apply skills they learn in human subjects' research, experimental testing, data collection and processing, statistical analysis, and FE modeling with a brain model to derive conclusions and a better understanding of head kinematics and TBI risk in sports and everyday activities.

Location: Wake Forest Baptist Health

Joel Stitzel, PhD
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Vertebral Strength and Injury Risk Following Long-Duration Spaceflight

Prolonged spaceflight can degrade the vertebrae and spinal muscles, leading to astronaut injury. This study is collecting pre- and post-flight CT and magnetic resonance imaging (MRI) scans of astronauts to quantify vertebral BMD, cortex thickness, geometry, and spinal muscle volume changes in 6-month space missions. Vertebral strength and injury risk will be quantified from simulations with a human body model altered to represent each astronaut’s pre- and post-flight vertebrae and spinal muscles.

The student will: 1) review literature on astronaut musculoskeletal deconditioning and form a hypothesis to test the effect of spaceflight on a bone or muscle outcome, and 2) learn image segmentation and registration, BMD and cortical thickness algorithms, and FE modeling to analyze pre- to post-flight changes in the astronauts to improve our understanding of injury risks associated with spaceflight deconditioning.

Location: Wake Forest Baptist Health

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Effect of High Protein Weight Loss Diet on Older Adult Bone Health

Weight loss is controversial in older adults due to its association with bone loss and increased fracture risk. This clinical trial aims to determine whether a high protein diet during and following weight loss will reduce loss of bone mineral density, bone thickness, and bone strength and decrease fat cells in the bone marrow in older adults with obesity. CT scans of 225 older adults randomized to low vs. high protein weight loss diets will be analyzed to quantify bone health. Subject-specific finite element models created from the CT data will be used to predict femur and vertebra strength and fracture risk.

The student working on this project will be trained in image segmentation, image registration, pipelines for quantifying bone quality (i.e. cortical thickness, bone mineral density), and finite element modeling and simulation. The student will form a hypothesis to test the effects of nutrition and weight loss on bone. To test the hypothesis, CT of participants will be analyzed to measure the changes that occur from baseline, 6-month, and 18-month CT scans.

Location: Wake Forest Baptist Health

Ashley Weaver, PhD

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Due to rising concern of head impact exposure and concussion in the 21 million children involved in team sports, this project aims to examine the biomechanical basis of sub-concussive and concussive head impact exposure in adolescent athletes instrumented with helmet-mounted and mouthpiece sensors.

The student will: 1) review literature focused on cumulative exposure of sub-concussive and concussive head impacts and factors influencing exposure (e.g. coaching techniques; practice and game guidelines/rules; community-based interventions; athlete age, size, experience, and position), and 2) design a hypothesis-driven experiment to examine analytically and computationally-based metrics of head impact exposure using FE modeling, on-field video analysis, biomechanical data processing, and statistical approaches learned from mentored training. The student will directly contribute to the broader research goal of reducing sub-concussive and concussive head impact exposure to improve sport safety in adolescents.

Location:

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Project 13

Image-based biophysical modeling to differentiate radiation-induced injury from tumor recurrence following stereotactic radiosurgery

Patients with intracranial metastasis treated with stereotactic radiosurgery (SRS) are evaluated for local control using serial MR imaging. Lesions can often be seen during these follow-up imaging sessions with expanding areas of contrast enhancement and surrounding tissue abnormality. Determining the underlying pathology of the lesion presents enormous clinical challenges as tumor recurrence and radiation-induced injury appear radiographically similar. Lesions are often classified as indeterminate and monitored with additional and costly serial follow-up imaging, at the risk of letting a potential recurrent tumor progress. New methods are desperately needed to guide therapeutic intervention decision-making in this important patient group. This project investigates the development of computational modeling methods that are driven by clinical imaging data. As the underlying physiology of the two conditions is fundamentally different, biophysical models may allow parameterization of lesion properties as a model-based biomarker to determine post-SRS enhancing lesion etiology, reducing costs due to unnecessary imaging or missed diagnosis.

The student will gain experience with medical image processing (segmentation, registration) and biophysical finite element modeling based on MRI data. The student will develop and deploy computational analysis pipelines and contribute to the development of computational model-based image analysis methodologies to guide interventional therapy for cancer patients.

Location: Wake Forest Baptist Health

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Quantifying Postural Differences in Patients with Low Back Injury

Lumbar disc herniation from automotive crashes, sports, and workplace injury can lead to recurring back pain. Postural training is a proposed alternative to surgical treatment of lumbar disc injury. This project aims to quantify postural differences between controls and low back injury patients that may be remedied through postural corrective therapies. Subjects will undergo biomechanical monitoring for up to 12 hours to quantify posture during normal activities.

The student will: 1) review literature on the postural effects of low back injury, posture sensing technologies, and postural therapies, 2) form a hypothesis to be tested through collection of postural data from control and injured subjects using a monitoring system, and 3) statistically analyze the monitoring results and identify key postural differences in low back injury patients.

Location: Wake Forest Baptist Health

Kerry Danelson, PhD
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The student will:

1. Review literature on impact-induced changes in the brain that are measurable with neuroimaging and cognitive testing, and
2. Develop a hypothesis-driven project to correlate neuroimaging measures, cognitive testing, and biomechanical head impact data in youth football players.

The student will be trained in multimodal imaging acquisition and analysis (diffusion tensor imaging, functional MRI, arterial spin label imaging, susceptibility weighted imaging, magnetoencephalography), cognitive testing, biomechanical instrumentation (helmet-mounted accelerometers), and statistical analysis. They will apply these skills in their project to analyze youth football data to identify neuroimaging and cognitive biomarkers that are sensitive to cumulative sub-concussive head impact exposure in youth football.

**Location:**

Wake Forest Baptist Health

Christopher T. Whitlow, MD, PhD, MHA

Chief of Neuroradiology and Vice Chair for Informatics
Director, Radiology Informatics and Image Processing Laboratory (RIIPL)
Director, CTSI Translational Imaging Program
Director, Combined MD/PhD Program
Departments of Radiology and Biomedical Engineering
Clinical and Translational Sciences Institute (CTSI)
Wake Forest School of Medicine
Automated Image Analysis System to Learn Bladder Anatomy

Normal bladder anatomy consists of several layers of tissue – urothelium (U), consisting of multiple layers of epithelial cells and resting on a basement membrane, lamina propria (LP), connective tissue which includes blood vessels and leukocytes, and muscularis propria (MP), a thick layer of smooth muscle which is covered by a layer of perivesical connective tissue of fat, blood vessels, and nerve bundles. T1 bladder cancer is defined as a tumor that has grown into the lamina propria under urothelium of the bladder but has not reached further down into the muscularis propria in the bladder wall. Several studies suggest that patient prognosis varies considerably when comparing superficial penetration into LP to deep penetration of LP. However, prevailing literature suggests that pathologists struggle to properly recognize invasion into LP due to limitations such as anatomical variability, tissue size, fragmentation, and processing artifacts. To enhance pathologic interpretation, we are developing an automated image analysis system to identify bladder layers from tissue biopsies and to measure the extent of LP invasion.

The student working on this project will implement the first part of this image analysis system to identify bladder layers using deep learning methodologies including data pre-processing, generation, artificial neural networks, and cross-validation through a machine learning paradigm know as conditional generative adversarial networks. This task will be executed on a high performance computing cluster using machine learning package of the student’s choice and Python or C. The student will work closely with pathologists to understand the microscopic anatomy of the bladder as well as the nature of the underlying disease state and staging protocols. The findings of this study may lead to a publication in a medical imaging conference.

Location:

Metin Gurcan, PhD

Director, Center for Biomedical Informatics
Professor, Department of Internal Medicine
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https://school.wakehealth.edu/Research/Institutes-and-Centers/Center-for-Biomedical-Informatics
Multiple instance learning (MIL) is a general, weakly supervised machine learning technique in which class labels (patient outcome) are assigned to collections of patterns ('bags') instead of individual instances (annotated regions for a certain landmark) of a class. In its simplest form (binary classification), it consists of two bags – one bag is labeled negative where every instance inside it is negative, and the other bag is labeled positive, where it contains at least one positive instance. For example, if a negative bag contains features or images corresponding to the negative class, then a positive bag contains the same kinds of images or features in addition to features or images of the positive class. Only the negative bag requires strictly instances of its own class, whereas the positive bag requires at least one instance of the positive class. Our lab is interested in applying multiple instance learning in conjunction with deep learning to identify T1 bladder cancer patients who are at a high risk of progression to a higher stage.

The student working on this project will create a deep learning implementation of multiple instance learning. This project will involve heavy use of machine learning packages in either Python or C, data augmentation, and basic image analysis methods on a high performance computing cluster environment. The student will work closely with pathologists to understand bladder cancer by learning microscopic anatomy of the bladder, underlying disease state, and staging protocols. The findings of this study may lead to a publication in a medical imaging conference.
Sarcopenic Opportunistic CT Metric Correlation with Motor Vehicle Crash Outcomes

Sarcopenia manifests in imaging as generalized muscle atrophy and fat infiltration, and is a strong predictor of mortality after trauma patients are discharged. With over 80 million CT scans performed annually in the U.S., opportunistic sarcopenia screening can identify vital risk factors to inform patient treatment. This project will examine CT-acquired muscle and adipose metrics in relation to patient outcomes in 800+ motor vehicle crash occupants in the Crash Injury Research and Engineering Network (CIREN).

The student will: 1) attend CIREN case reviews where engineers and physicians analyze crash, radiology, and medical evidence to determine occupant injury mechanisms, 2) review manual and automated CT methods for measuring sarcopenia, and literature correlating sarcopenia to trauma outcomes, and 3) design and conduct a hypothesis-driven project to determine the relationship between CT-derived sarcopenia metrics (densities and cross-sectional areas of muscle, visceral fat, and subcutaneous fat) and CIREN occupant outcomes (e.g. days hospitalized, ventilator days, mortality, functional health). The student’s contributions will lead to automated CT algorithms for sarcopenia characterization, and screening techniques to identify trauma patients at high risk for adverse outcomes.

Location: Wake Forest Baptist Health

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Prevention of Radiation Therapy-Induced Fractures

Cancer survivors increasingly experience skeletal fractures following radiation therapy (RT), as demonstrated by increased femoral neck and pelvic fractures in postmenopausal women irradiated for cervical (+66%), rectal (+65%), and anal (+216%) cancers by five years post-RT. An early increase in active bone resorption by osteoclasts occurs after RT, which persists and likely leads to fractures. However, no interventions exist because of toxicities associated with antiresorptive therapies and RT, including osteoradionecrosis. This project will determine if a novel compound, 4µ8c, is a well-tolerated, translatable intervention to prevent radiation-induced osteoclast activity, differentiation, and bone loss. 4µ8c inhibits the activity of inositol requiring ER-to-nucleus signal kinase-1 (IRE-1α), which enhances osteoclast differentiation and activity.

The student will: 1) review literature on the effects of RT, 4µ8c, and IRE-1α on osteocytes, and learn about bone remodeling assays (molecular, biochemical, imaging, biomechanical), 2) design a hypothesis-driven study to determine if pretreatment with 4µ8c prevents RT-induced osteoclast differentiation and activity in vitro, and vivo, and 3) perform molecular, cytologic, resorption, microCT, and biomechanical experiments to test the hypothesis and draw conclusions to inform treatment recommendations to prevent RT-induced bone loss and fracture.

Location: Wake Forest Baptist Health

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Networked Data Models

Electronic Medical Records (EMRs) are aimed at supporting clinical practice at the point of care. These are often deeply customized and unique to the institutions in which they operate. Therefore, when conducting research with collaborators at other institutions it is often difficult to execute systematic analysis of these disparate observational databases. Common Data Models (CDMs) allow transformation of data contained within these databases into a common format as well as a common representation (terminologies, vocabularies, coding schemes), which then allows systematic analyses using a library of standard analytic routines that have been written based on the common format. The CTSI at Wake Forest leads and participates in several of these regional and national networks sharing data for basic science, retrospective studies, and clinical trial recruitment.

The student working on this project will be trained in data analytics and supporting application programming. The student will get familiarity with national medical data standards, ontological systems, and the full-cycle process of research from cohort identification to data extraction and analysis. Data characterization, cleaning, Natural Language Processing (NLP), and visualization will be explored. Prior experience with application programming, databases, and statistics is helpful.

Location: Wake Forest School of Medicine

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Informatics Techniques to Learn From Big Healthcare Data

Clinicians and Informaticians all over the country are working to make healthcare smarter and establish Learning Healthcare Systems. We are doing this by gathering data produced by clinical practice and applying analytics methods to learn about diseases and care processes. However, naïve analysis can yield misleading results because clinical data are not perfect. In this project you will have an opportunity to go beyond the analysis approaches that can be learned through online courses. You may even get to develop your own methods for data analysis and quality assessment. Most importantly, you will learn about the pitfalls of reusing clinical data. This first experience in clinical research informatics will prepare you for medical school, graduate school or even a career in healthcare data science.

The students working on this project will be trained in clinical research informatics and secondary use of clinical data. No coding experience is required as qualitative analysis projects can be defined based on each student’s interest. Pervious students have developed whole data analytics modules using R, developed natural language processing modules in python and developed machine learning pipelines. Students will also be able learn hands on skills such as data wrangling, cleaning and analysis using python, R, SAS or SPSS as well as research skills such as experiment design and qualitative analysis.

Location: Wake Forest School of Medicine

Franck Diaz, PhD
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ICU Medication Safety

The overarching goal is to use data from the electronic health record and smart infusion pumps to detect potential errors in the administration of high-risk medications. This work has been in process since 2011 at Cincinnati Children’s Hospital Medical Center (CCHMC), the former institution of the Principal Investigator, Dr. Eric Kirkendall. Dr. Kirkendall continues to lead the team at CCHMC and is working to spread the work to Wake Forest Baptist Medical Center.

Aim 1: R01-funded work to compare NICU medication order and Medication Administration Record (MAR) data in real-time and notify clinicians when there is a discrepancy (possible error).

Aim 2: Studying the portability of the work into other NICUs and adult ICU settings.

Aim 3: Incorporating smart infusion pump data into Med Administration error detection algorithms, so could compare order, med administration record (MAR) and smart pump data.

The student who joins our team will learn and/or perform one or more of the following activities:

• Cleaning and preparation of large datasets
• Basic and advanced data analytics
• Software prototyping & development
• Software implementation and evaluation
• IRB application & manuscript preparation

Location: Wake Forest School of Medicine

Eric Kirkendall, MD, MBI

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https://school.wakehealth.edu/Research/Institutes-and-Centers/Center-for-Healthcare-Innovation
Project 23

Development of Theranostic Nanoparticles for Improved Tumor Detection and Treatment

The implementation of the innovative technologies remains the top priority for the development of potential modalities for the diagnosis and treatment of various cancers. Despite all the recent advances, some recalcitrant tumors, i.e. pancreatic, ovarian, etc., remain poorly diagnosed until late stage resulting in limited opportunities for patient cure. Because of the few apparent early symptoms, significant effort will be made for developing efficient methods to identify and target recalcitrant cancers. This project will develop actively targeted nanoparticles containing a tumor specific gatekeeper and targeting moiety to deliver contrast agents and drugs to tumors. Tumor specific delivery in vivo will be evaluated utilizing a new imaging technology, Multispectral optoacoustic tomography (MSOT).

The student working on this project will construct a tumor targeted nanoparticles, characterize the nanoparticles, evaluate tumor specificity of the particles, test nanoparticle efficacy, and participate in multispectral optoacoustic tomography imaging. The students may participate in image analysis and evaluation of pharmacokinetics.

Location: Wake Forest Baptist Health

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