

SIR Foundation Summer Medical Student Internship Program

Institution Name: Northwestern University

Responsible mentoring physician: Robert J Lewandowski, MD, FSIR

Length of proposed curriculum: The internship should be 8 weeks and at least 40 hours per week.

A. Please provide a brief description of how each of the following curriculum elements will be demonstrated/taught through your program.

During the proposed summer medical internship program, trainee(s) will spend most of their time in dedicated research-related training with our Interventional Oncology group. This training will include laboratory bench work, preclinical animal research, group meetings, seminars, research conference attendance, journal clubs, and clinical conferences relevant to their research pursuits.

The Interventional Oncology group at Northwestern University is a well-developed research enterprise with both clinical and preclinical research activities. The clinical arm includes nursing staff, medical students, residents, fellows, and clinical support staff dedicated to interventional oncology. This group works closely with a highly productive preclinical translational research lab run by Dr. Dong-Hyun Kim. The trainee(s) research goals will be accomplished by weekly formal and informal meetings with the mentoring physician, interactions with post-doctoral fellows and graduate students, and group meeting presentations once per month. Weekly group meetings focus on critical interpretation of data, research methods, and future directions. Our IO group is extremely interdisciplinary, with experts in magnetic resonance imaging, biophysics, biomedical and electrical engineering as well as clinical experts in fields of medical oncology, interventional radiology and pathology. It is expected trainee(s) will benefit from discussion and collaboration amongst lab group members as they proceed with their research over the course of the summer.

The overall goals of Dr. Kim's laboratory are focused on developing various therapeutic/imaging carriers for the treatment of cancers. Micro/Nanoparticles and their hybrid derivatives have been exploited as vectors for drug/therapeutic delivery and molecular imaging agents. We are working closely with clinicians, medical scientists, biologist and imaging professionals to translate new therapeutic approaches using various multifunctional carriers and diagnostic imaging technique to the clinical setting to significantly improve the imaging and treatment of cancer.

This research experience will give trainee(s) the opportunity to generate a hypothesis (concept development) under direct guidance, test it, and evaluate the results. Though the mentoring physician will supervise all aspects of the project, it will be the trainee(s) responsibility to ultimately perform the requisite experiments for study and analyze the results with assistance as needed. Trainee(s) will receive instruction in experimental methodology (data collection, statistics, and data analysis) and additional support (from graduate students, medical students, residents, and fellows, etc) as needed to conduct their research.

The expectation for trainee(s) will be to craft a Scholarly Abstract for the Annual Medical Scholars Research Day and for trainee(s) to have an abstract submission for the Annual Scientific Meeting of the Society of Interventional Radiology with a well-written manuscript in submission at that time.

B. Please provide the details on the instructional setting and methodology (laboratory, classroom), description of any educational resources (PowerPoint presentations, textbooks, selected readings), and assessment techniques (question and answer sessions, tests) to be used in the process of instruction.

Resorbable Analgesic Microsphere Embolization in the VX2 Rabbit Model of Uterine Fibroids

Uterine fibroid embolization (UFE) is an effective therapy for the treatment of symptomatic uterine fibroids, but significant post-procedural pain is common. Some have advocated intra-arterial lidocaine or nerve blocks to ameliorate pain in these patients, but these interventions have limited success and carry increased risk of cardiac arrhythmia or require a separate additional procedure, respectively. The currently implemented embolic microspheres for UFE have no analgesic properties. Our team seeks to implement novel resorbable analgesic microsphere (RAMs) loaded with CB1 receptor agonist. The uterus has high CB1 receptor expression, which has been implicated in promotion of myometrial relaxation based on biopsy specimens after C-section with low levels of CB1 receptors in adenomyosis where uterine hypercontractility may play a role in pain. This pilot study seeks to examine the safety and feasibility of administering CB1 receptor agonist eluting microspheres in a rabbit model of uterine fibroids.

- Aim 1: Synthesis and fabrication of imageable resorbable analgesic microspheres (RAMs) with microfluidic techniques
 - Task 1-Optimization of analgesic drug loading properties and sizing
 - Task 2-Characterization of microsphere degradation
 - Task 3-MRI relaxometry of imageable microspheres
- Aim 2: Validation of MRI-based perfusion metrics and imaging response assessments in VX2 rabbit model of uterine fibroids
 - Task 1-Creation of VX2 uterine fibroid rabbit model

- Task 2-Optimization of MRI pulse sequences for evaluation of VX2 uterine fibroid tumor response
- Task 3-Compare transcatheter intra-arterial perfusion (TRIP) MRI metrics of fibroid perfusion compared to conventional CT perfusion
- Aim 3: Evaluation of microsphere biodistribution and laboratory toxicity
 - Task 1-Evaluate toxicity with laboratory blood tests after UFE with RAMs
 - Task 2-Semi-quantitative analysis of microsphere biodistribution within target (fibroid, uterus) and non-target (heart, spleen, lungs, brain, liver, kidneys, GI tract) tissues
 - Task 3-Compare transcatheter intra-arterial perfusion (TRIP) MRI metrics of fibroid perfusion compared to conventional CT perfusion
- Aim 4: Assessment of fibroid response and rabbit pain
 - Task 1-Assess fibroid perfusion after UFE with RAMs
 - Task 2-Evaluate changes in rabbit pain with Rabbit Grimace Scale after UFE with RAMs

In Vivo Characterization of Transarterial Particulate Steroid Embolization in a Rat Model for Musculoskeletal Applications

Genicular artery embolization (GAE) is an effective and durable investigational, minimally invasive therapy for reducing knee pain related to osteoarthritis. Additional areas of investigation include intra-arterial embolization for adhesive capsulitis of the shoulder. However, no embolic agents have been optimized or approved for musculoskeletal applications. Intra-arterial administration of particulate steroids have been shown to result in microvascular occlusion secondary to red blood cell aggregation and spiculation. This pilot study seeks to evaluate peripheral ischemic changes after intra-arterial particulate steroid embolization in rat kidney.

- Aim 1: To optimize steroid particulate composition for intra-arterial delivery
 - Task 1-Optimization of particulate steroid dosing
 - Task 2-Selection of particulate size for intra-arterial applications
- Aim 2: To compare DSA perfusion and toxicity in steroid- vs non-steroid particulate embolization in native rat kidney
 - Task 1-Comparison of semi-quantitative scoring of renal artery perfusion pre- and 2d post-embolization
 - Task 2-Evaluation of laboratory blood tests for toxicity after embolization
- Aim 3: To evaluate histopathological changes (H&E) and biodistribution after steroid- vs non-steroid particulate embolization in native rat kidney
 - Task 1-Com

C. Please provide a brief outline of available research topics, one of which the student will select for completion as part of the program. The projects should be of a scope appropriate for completion within the limited time frame provided.

In addition to pre-clinical laboratory research studies, trainee(s) will also have the opportunity to observe clinical procedures (facilitated by the mentoring physician), shadow in interventional oncology clinic, and attend a weekly multi-disciplinary liver tumor board conference (with interventional radiology, medical oncology, hepatology, and transplant surgery). These experiences will provide clear translational relevance to trainee(s) research focus permitting firsthand observations of how research efforts could one day impact in the lives of these patients.

At Northwestern, trainee(s) will have the opportunity to attend seminars by world-class speakers in interventional radiology, radiology, biomedical engineering, chemical and biological engineering, cancer research, chemistry, and other department colloquia. Trainee(s) will be encouraged to attend seminars that are relevant to their research and to expand their exposure to radiology and perspective throughout training.