BIOE477/598DP

Team:
Team members:

This is a team activity (Total points: 100).

Choose a topic of your interest from the list below.

Final Project Topics

Topic-1: Development of a multiplex molecular imaging technique for early detection of prostate cancer. Various molecular markers present different capacities in early detection of prostate cancer and predict disease course. However, none of the current markers individually are able to provide precise diagnosis and discriminate accurately between normal, early stage and aggressive cancers. Simultaneous detection of multiple indicators of this disease's presence and progression are highly desired to provide more efficient early stage diagnosis, predict disease course, and eventually administer effective therapy. The purpose of this research is to develop a molecular imaging technique which is able to detect two or more molecular markers simultaneously and provide a long-term strategy to study multiplex molecular imaging and create targeted probes to antigens expressed by prostate cancer. A long-term overarching strategy is to obtain nearly 100% accurate diagnosis using molecular imaging techniques with high magnitude (μM level) than offered currently using direct MRI/ultrasound imaging techniques (μM-MM level).
The specific aims of this project are: 1) investigate the molecular pathology of prostate cancer and identify the effective diagnostic biomarkers. 2) Identify and design multiple biocompatible probes targeted to prostate cancer antigens. 5) Design validation experiment of the multiplex molecular imaging.

Topic-2: Development of a next generation image-guided liver cancer therapy for Transcatheter arterial chemoembolization (TACE). Liver cancer is one of the most common cancers with ~500,000 new cases/yr of hepatocellular carcinoma (HCC, primary liver cancer) and >200,000 new cases/yr of liver dominant colorectal cancer metastases (secondary liver cancer) worldwide. Treatment options are limited, and clinical outcomes are generally poor with a median survival rate of less than one year. Given the fact that liver cancer (primary and metastatic) is primarily supplied by the hepatic artery and is generally confined to the liver, drug delivery directly into the hepatic artery has been shown to be effective in the management of these patients. Transcatheter arterial chemoembolization (TACE) is an x-ray imaged guided, interventional oncology procedure in which chemotherapeutic drug is delivered from a catheter in the hepatic artery and considered as mainstay of intermediate stage HCC therapy. Recently, there has been a shift in the chemotherapeutic drug delivery system from the conventional lipiodoldoxorubicin cocktail (c-TACE) to drug-eluting microsphere beads (DEB-TACE). DEBs are capable of delivering chemotherapeutic agents in a reproducible manner that

leads to negligible levels of chemotherapy in plasma (less systemic exposure) and enhanced efficacy at the tumor site. Despite these successes, DEB-TACE rely heavily on clinician experience and further confounded by the fact that DEBs are radio-lucent under standard integrating detector type x-ray systems (C-arms). X-ray contrast medium is mixed with the DEBs for better visualization during injection. However, differing fluid dynamic properties of the two materials make them prone to separate. This can result in non-target drug delivery and a high recurrence rate (either due to incomplete tumor kill or partial treatment). DEBs (100-300 microns in diameter) loaded with x-ray opaque materials (e.g. lipiodol; imageable DEBS, i-DEB) are only visible when large concentrations are at virtual stasis which is likely not useful clinically. Despite these efforts, the risk of developing severe infectious complications such as an abscess within the necrotic tissue, hemorrhage, septicemia and cholecystitis are very common. Patients may develop hyperthyroidism (with iodinated agents), allergic reaction or toxicity (from the microbeads) due to the use of the contrast media. Clearly, the unmet need is a modality sensitive embolic strategy that will penetrate and block even very small vessels within the tumor but unlike liquid embolic agents, such as ethanol or acrylic, and microparticulate agents, greatly limit the damage to adjacent normal tissue.

The specific aims of this proposal are: 1) Design and develop a thermoresponsive, modality-specific chemo-occluding agent for therapeutic chemoembolization. 2) Investigate rheological and mechanical properties of the agent on blood viscosity and flow and blockage with fluoroscopic X-ray and conventional CT imaging in vivo. 3) Design validation experiment to confirm effective chemo-occlusion, therapeutic efficacy and safety in vivo.

Notes:

- Your idea should be original and never should have been published anywhere else.
- You should provide enough details to approach this problem.
- There will be a written report of 3 pages (Arial, 11 font, single spacing, 0.5 margin). Written report should have the following sections- i) Background and Significance; ii) Approach; iii) Innovation; iv) Design of experiments.
- If any of you are interested in taking up a hands-on project, please let me know.