CBNS Animal Imaging Workshop
Practical

Over two days you will take part in experiments to see the practical work involved in the two major types of imaging studies: biodistribution and therapeutic efficacy. We will look at the different modalities available for answering questions in each experiment type and through the acquisition of data and processing we will examine the information you can get beyond the images themselves.

– Day 1: Biodistribution –

Multimodal Validation of Biodistribution

Case Study Summary:

You have made two new structurally similar nanocarriers: one with a chelator for radiochemical (PET) detection and the other with a dye for optical (fluorescence) detection. The material is novel and is ultimately intended for drug delivery, but the biological distribution, circulation half-life, and clearance pathways are all unknown for the new material. Using both modalities how can we develop an experiment to determine these properties?

Experimental Description:	The biodistribution and tumour accumulation of a ^{89}Zr and cynanine-5 (Cy5) labelled nanocarrier will be measured using PET and optical techniques *in vivo* and validated *ex vivo*.
Key Questions	• Which method is quantitative, and which one isn't? • How can the two imaging modalities be used together to gain more information? • Which method is higher throughput? • How could we calculate the biological half-life of the material? • What is the major clearance path for the material? Is this consistent with the expected clearance based on the materials properties? Is this confirmed by both techniques? • Are there differences in the biodistribution between the two materials?
Image Processing	• PET-CT ROI Analysis • Ex Vivo ROI Analysis • Spectral Unmixing • Correlation between *in vivo* and *ex vivo* data.

Notes:

– DAY 2: IMAGE GUIDED THERAPEUTICS –

UNDERSTANDING DISEASE STATE WITH PET-MRI AND OPTICAL IMAGING TO EVALUATE THERAPEUTIC EFFICACY

Case Study Summary:

You have a new carrier that is designed to release drug for treatment of a brain tumour, and you want to test how effective this polymer is at treating the tumour. Because the tumour is internal you need to know the accessibility of the tumour from the bloodstream as well as how effective your treatment will be once it gets there and the distribution of the drug in the tumour tissue. What experiments can we do to determine if the tumour is vascularised enough to allow your nanocarrier to permeate into the tumour space as well as the distribution of both the carrier and the drug in the tumour microenvironment?

Experimental Description:	**Experiment 1:** ^{18}FDG & Gadovist® will be co-injected in a mouse with a brain tumour and the uptake into the tumour will be monitored using PET and MRI over a short time. A variety of MRI acquisitions will be taken, and the types of tissue contrast you can see and information you can obtain with and without contrast agents will be explored. In particular we will look at physiological disease state and get information on wash in and wash out rates of a tracer. **Experiment 2:** A carrier with a non-cleavable dye (Cy5) on the polymer and cleavable doxorubicin has been administered to mice. In order to see the drug distribution *in vivo* and in the tumour microenvironment imaging will be done and followed by *ex vivo* analysis of the tumour. In addition, the health of the mice will be examined after treatment and the toxicity of the treatment will be assessed with *in vitro* techniques from collected blood.
Key Questions	• Which tracer is better for pharmacokinetic analysis? • What kinds of information can you obtain from the different MRI sequences? • Why use PET if Gadovist® can give pharmacokinetic information? • Could we track the drug information we get from fluorescence in PET? • Can we do kinetic analysis via fluorescence? • Can we do multi-probe imaging with PET like in fluorescence?
Image Processing	• Benefits and issues of co-registration • Kinetic Analysis (with MRI and PET) • Anatomical features • Drug distribution

Notes: