Molecular imaging of biological systems will provide information on soft tissue structure and function without resorting to invasive investigative procedures.

Our focus of research is in chemistry for positron emission tomography (PET) imaging, since PET will be one of the primary tools for the diagnosis of cancer and for the monitoring of the effects of therapy. Copper-64 is of interest as it is both beta and positron emitter, thus offering the possibility of simultaneous imaging and therapy.

In our work tumour delivery takes place via two routes: (a) using the intrinsic properties of the small-molecule based probe (via hypoxic selective metallic complexes); (b) using ‘targeted’ delivery to the surface of cancer cells via bioconjugation to an ‘address’ (e.g. nitroimidazoles for hypoxia targeting).

Thus far, we achieved the successful synthesis of highly kinetically and thermodynamically stable compounds including the demonstration of the first use of Cu(I) for imaging purposes. This is a significant step forward in the development of Cu-based imaging agents. Crucially, we obtained simultaneously fluorescent and radiolabelled Cu(II) molecules having the ability to act as synthetic platform for imaging drugs targeting hypoxia. We can now couple copper coordination chemistry with fluorescence imaging and spectroelectrochemistry to study the redox switching of fluorescence under hypoxic conditions (i.e. in poorly oxygenated tumours). We will next establish the effects that different numbers of targeting groups, charge and lipophilicity have on cell targeting and biodistribution. Importantly, we discovered new tailor-made fluorescent coatings for SWNTs. This will now enable us to derivatise these nanocomposites with biomolecules capable of hypoxia targeting. In an alternative approach to drug delivery we use reversible covalent bonding to construct nanocapsules and nanovesicles. Crucially, we synthesised and characterised new tripod building blocks for such nanocapsules, which will enable us to test the controlled-release of imaging agents under pH and redox control. High yielding radiolabelling protocols and in vitro studies (both on ‘cold’ and on radiolabelled species) for cellular uptake are in progress. The development of new imaging probes suitable as synthetic platforms for multimodal imaging techniques (PET/optical imaging) is underway. A general method for the targeted delivery of imaging reagents, leading to detailed information on the nature of biological processes in cells and animal models will emerge.

The synthetic and characterisation work would not have been possible without the support and assistance from the specialised team at the National MS Service since 2005. Therefore NMSSC has not only helped our research but it has become an indispensable and key tool towards achieving our research aims, which are the development of new imaging agents for hypoxia.

References: