Marie Curie Career Integration Grant Final Report

Molecular Imaging of Redox Processes in Cancer *"ImagingRedox"*

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Over the past four years, I have successfully re-integrated within the European Union following my overseas postdoctoral training in the USA. I have built a team that operates between the Department of Physics and Cancer Research UK Institute at the University of Cambridge, with active research staff, laboratory space and infrastructure in both locations. My multidisciplinary team now has 18 members from diverse backgrounds, including: molecular biology; chemistry; engineering and physics; as well as collaborators across the physical and biomedical sciences.

My research programme unites: **modelling**, to better understand and characterise the interactions between light and tissue; **innovative optical instrument design** (Figure 1), integrating new technologies to enable spectroscopic imaging of complex biological dynamics; and **translational research methods**, applying these techniques to reveal new biology in animal models of cancer and ultimately performing clinical trials in patients. Our multidisciplinary breadth allows us to accelerate translation of innovations from the Department of Physics, through preclinical assessment at the CRUK Cambridge Institute and into clinical trials at Addenbrooke's Hospital (3 clinical trials completed; 2 recently approved).

Summary of the Results

Our research achievements can be broadly divided into two main themes: technology and methodology innovation for cancer imaging; and shedding new light on oxidative stress and oxygenation in cancer. These themes interplay closely, since a lack of tools to reveal oxidative stress and oxygenation in living systems stimulates technology innovation, while technical validation of new tools enables their application to address research questions in biomedicine.

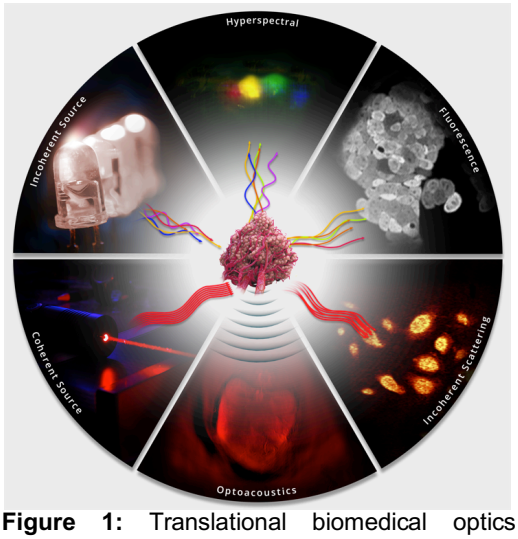

Figure 1: Translational biomedical optics actively under development and clinical

Highlights of our achievements in technology and methodology innovation during the grant period include:

- Design, development and biological validation of novel endoscopy instruments to resolve early microstructural (holographic imaging) and biochemical (hyperspectral imaging) changes during cancer evolution for application in the gastrointestinal tract;
- Development of novel photoacoustic imaging techniques, including oxygen-enhanced imaging to detect vascular function and an activatable contrast agent for detection of hydrogen peroxide at low concentrations in tumours;
- Technical and preclinical biological validation of both imaging tools to enable clinical trials in *ex vivo* tissue and *in vivo* in human patients.

Highlights of our achievements in the study of oxidative stress and oxygenation in cancer include the application of:

- Raman spectroscopy to detect the indirect effects of reactive oxygen species in cells and tissues from the lung, including oxidative damage to proteins and lipids;
- Hyperspectral imaging to evaluate changes in tumour haemoglobin concentration and oxygenation during cancer progression in mouse models of breast and prostate cancer;
- Photoacoustic imaging to detect hydrogen peroxide formation in response to doxorubicin in mouse models of breast cancer and to detect haemoglobin in breast cancer patients for differentiation of benign and malignant breast lesions.

Socio-Economic Impacts

Stakeholders in this research are numerous: academics; imaging instrument manufacturers; endoscopists and radiologists; pathologists and surgeons; healthcare systems; patients and the general public. We have achieved academic impact through our publications and conference presentations, leading to a further £4.1M of grant funding. We have built active collaborations with instrument manufacturers in UK, Germany, Netherlands, Belgium and Japan. We have engaged clinicians in quarterly project meetings. We work with our Office for Translational Research to engage the NHS. We regularly consult patient advocates and are highly active in public engagement activities (see facebook). Importantly, the results of this research have already been used to inform clinical trials in breast and oesophageal cancer patients.