PhD Project Proposal

PhD Project Title	**MultiSpectral Endoscopy (MuSE) for early cancer detection**
Primary Supervisor & Department	Professor Sarah Bohndiek, Department of Physics
Second supervisor (if applicable)	Dr Massimiliano di Pietro, Addenbrookes Hospital

Project Outline	**Motivation** Each year in the UK, over 55,000 patients will be diagnosed with oesophageal or lung cancer; a staggering 44,000 will die from their disease[1]. The majority of patients are currently diagnosed when their disease is at a late stage (with regional or distant spread), yielding less than 10% survival over 5 years[1]. Therefore, a key clinical unmet need remains for early disease diagnosis. For this PhD project, the student will exploit the fact that many cancers of the gastrointestinal tract and lung emerge from abnormal (dysplastic) precursor lesions[2] and by improving approaches to detect these endoscopically, facilitate early curative intervention[3]. **Current Status** In the VISIONLab (http://www.bohndieklab.org/), we have recently reported several exciting new endoscopic imaging tools that could help to shed light on dysplastic lesions[4–6]. In unpublished work, we have also undertaken clinical trials using some of these tools, applied to both excised tissue from patients but also excitingly in first-in-human trials together with our colleague Dr Massimiliano di Pietro, who guides our clinical activities and will co-supervise this project. These studies have enabled us to gain a better understanding of how the multiple optical interactions that occur when light is incident on biological tissue[7] are altered in different disease states of the oesophagus. **Aim and objectives of the proposed project** The overall aim of this project is to develop the next-generation of advanced endoscopic imaging tool to facilitate early cancer detection. Advancing on our latest findings using multispectral endoscopy in the oesophagus, the objectives of this PhD project are: 1. To design, build and validate a multispectral spatial frequency domain imaging (SFDI) system for tissue analysis that will enable extraction of tissue optical absorption and scattering in ex vivo samples; 2. To extend existing clinical trials and initiate new studies to image *ex vivo* samples from oesophageal tissues through our collaborators Dr di Pietro and Dr O'Donovan at Addenbrooke's Hospital and depending on suitable project progress, also with Drs Rintoul and Rassl at Papworth Hospital; 3. To incorporate the generated knowledge into a next-generation multidimensional endoscopy system, exploiting the current state-of-the-art in photonic multispectral filter arrays for chip-on-tip endoscopy emerging from the VISIONLab[8].

Project plan	**Methodology** The student will combine experimental characterisation of tissue optical properties with clinical tissue studies and novel endoscope design to achieve these goals. They will be required to undertake the following methods under each objective: Objective 1: • Design of a new illumination system to enable active wavelength selection as well as spatial patterning of the illumination, considering low-cost multispectral LED solutions as well as advanced projection systems. • Phantom fabrication to validate performance as a function of optical absorption and scattering content. • Develop our existing analysis code for multispectral analysis. Objective 2: • Acquire a research passport and work with biostatisticians and clinical colleagues to design an optimal study with histopathological co-registration of imaging data; • Develop containment level 2 tissue handling skills; • Conduct clinical studies and acquire optical data from a sufficient range of precursor lesions across different disease sites. Objective 3: • Identify candidate biomarkers based on existing literature and prior studies by our laboratory and evaluate these in data collected during Objective 2; • Learn the core skills of endoscopy design and use these to prepare an optical design for detection of the proposed biomarkers; • Construct an endoscopy prototype and test in phantoms as well as *ex vivo* tissues. **Novel content of the research** The project will generate new knowledge as to the optical interactions in precursor lesions that need to be identified for curative resection in early cancer detection in the aerodigestive tract. The design of a multispectral SFDI system will build on prior work in OpenSFDI but ultimately extend the capability of the illumination that these systems can provide. The multidimensional endoscopy capability will be enabled by state-of-the-art photonic filter designs. We also hope that advancing these new biophotonic approaches will enable new collaborations to form with groups across the CRUK Alliance for Cancer Early Detection, for example, with the de la Zerda lab at Stanford.
Main methods to be used	Endoscopy, Multispectral imaging, Spatial frequency domain imaging Data acquisition and hardware control, Image processing.
Key References	1. Cancer Research UK Statistics. http://www.cancerresearchuk.org. 2. Mannath, J. & Ragunath, K. Role of endoscopy in early oesophageal cancer. *Nat. Rev. Gastroenterol. Hepatol.* **13**, 720–730 (2016). 3. Sturm, M. B. & Wang, T. D. Emerging optical methods for surveillance of Barrett's oesophagus. *Gut* **64**, 1816–23 (2015). 4. Yoon, J., Joseph, J., Waterhouse, D. J., Luthman, A. S., Gordon, G. S. D., di Pietro, M., Januszewicz, W., Fitzgerald, R. C. & Bohndiek, S. E. A clinically translatable hyperspectral endoscopy (HySE) system for imaging the gastrointestinal tract. *Nat. Commun.* **10**, 1–13 (2019).

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