PhD Project Proposal

PhD Project Title	Artificial intelligence (AI) for automated early detection of renal cancer
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Second supervisor (if applicable)	Sam Stranks (Chemical Engineering & Biotechnology/Physics)

Project Outline

Aims and objectives

Cancer is a major public health problem worldwide that causes more than one in four deaths in the UK [1]. Computed tomography (CT) is the most commonly used imaging modality for detection, diagnosis and treatment follow-up. Thus, the development and deployment of CT-derived biomarkers is a major interest within the cancer research community. In particular, the development of AI tools for cancer research can help enormously in the assessment of radiological images, by significantly reducing its processing time, and also improving the sensitivity for tumour detection compared to the standard visual interpretation [2], this is particularly important when considering reporting of large volumes of CT scans in a screening context. In fact, to develop a leading role in AI is the NHS Long Term Plan [3].

Early detection is especially important for cancer types that present non-specific symptoms until a very advanced stage of the illness. One such malignancy is renal cell carcinoma (RCC) [4], the 7th commonest cancer in the UK with a 50% mortality rate. Overall 60% of patients present incidentally and 87% of all patients with curable small RCCs (i.e. <4cm).

The optimal method for achieving early detection at a population level is screening. Typically, contrast-enhanced CT (CECT) is used for optimal detection and characterisation of renal masses. Whilst tumour detection is easier in CECT, it is also possible, although more challenging, in non-contrast CT (NCCT), generally used for evaluation of renal stones. Low dose NCCT is currently being evaluated as a screening test for lung cancer in targeted lung health checks. Thus, there is the potential to detect renal tumours in tandem with these lung screening programmes using low dose NCCT scans of the abdomen. The deployment of an AI strategy for automated reading of these NCCT scans would be beneficial in terms of efficiency, man-power and cost effectiveness of a renal cancer screening programme.

Therefore, the aim of this proposal is to develop and validate such AI algorithms for automated detection of RCC on NCCT, to assess the feasibility of early detection of RCC with low dose CT in screening programmes.

Project plan	The plan for this project can be divided in two work packages (WP) WP1: Develop and validate AI algorithms for automated tumour detection on NCCT This WP includes the development of both (semi-)supervised and unsupervised AI algorithms for: a) Automated detection of renal masses on NCCT images, appropriately combining learned and handcrafted image features. b) Classification of the different RCC subtypes, finding correlations between histological classification and imaging features. WP2: Assessment of feasibility of early RCC detection in a screening context In this WP we will adapt and apply automated algorithms developed in WP1 to the CT images obtained in screening programmes to detect renal masses. These will be validated using the manual segmentations performed by expert radiologists. WP2 will be carried out in collaboration with the Yorkshire Kidney Screening Trial (YKST), a sub-study of the Yorkshire Lung Screening Trial (YLST, CI- G Stewart). The YLST programme uses mobile scanning vans for lung screening of Yorkshire residents at high risk of developing lung cancer. The aim of YKST is to assess the feasibility of adding an abdominal NCCT scan to the chest CT scans in participants of the YLST, that will allow screening for RCC. The YKST trial is now funded and expected to start recruiting in 2021, fitting very well the timeline of this PhD proposal, and it will be the first clinical trial worldwide with such a purpose. YKST will provide the first cost-effectiveness analysis of adding RCC screening (potentially other upper abdominal cancers also) to lung cancer screening. For this innovative trial, tools to automatically detect abdominal tumours in NCCT scans will need to be developed, which is more challenging than for CECT due to the lack of enhancement of the tumour. The algorithms and models for NCCT from WP1 will be incorporated in a software framework to automatically detect and segment renal masses from the trial mobile units. This will be done using the CRUK funded NCITA [5] repository and associated tools that are built and developed in the Radiology Department as part of the CRUK Cambridge Center Advanced Cancer Imaging Programme. The project will use the following patient cohorts: • Cohort 1: RCC (Cambridge University Hospitals (CUH) NHS Foundation Trust consisting of annotated (manually segmented) CECT segmented images for 300 patients who underwent nephrectomy at CUH (2014-2017). Additionally, the corresponding unenhanced images will be available for an estimated 200 of those patients. This cohort will be used in WP1. • Cohort 2: Abdominal NCCT images from screening, YKST cohort. This trial is expected to collect ~6200 abdominal screening images, with ~34 RCCs expected in total.

Main methods to be used	The main methods to be used for this project will be cutting-edge medical imaging analysis methods and tools; in addition, novel AI algorithms will be developed. Finding and classifying renal masses is a challenging problem in NCCT. Studies have shown that the main biomarkers that can be used to detect lesions on NCCT are: • Attenuation (of pixel intensity, in terms of Hounsfield Units), possibly due to the presence of microscopic fat within the tumor • Morphology: deformation of the renal contour • Texture: e.g. heterogeneity Each of these parameters has limitations when used alone, and state-of-the-art publications show that over one-third of potentially detectable cancers were missed when size was the only feature used [6]. A combination of those biomarkers via Machine Learning algorithms will be explored to improve detection. Other radiomic features will be used as well. Radiomics [7] provides quantitative measurements of tissue characteristics, such as shape or heterogeneity, that are also objective, reader independent non-invasive biomarkers, and can increase the accuracy of diagnosis and prognosis, and give insights to better predict clinical outcomes and treatment response [8]. In addition, unsupervised AI algorithms will be developed, leveraging latest DL algorithms and tools, such as neural networks [9]. Methods and algorithms will be developed in collaboration with mathematicians, physicists and computer scientists from both the Department of Radiology (supervised by Sala and Escudero), Department of Applied Mathematics and Theoretical Physics (DAMTP) and the Department of Chemical Engineering & Biotechnology/Physics where we already have extensive collaborations with Schoenlieb and Stranks groups.
Key References	[1]Cancer Research UK, https://www.cancerresearchuk.org/health-professional/cancer-statistics/, Accessed July 2020. [2] Shen, L., Margolies, L.R., Rothstein, J.H. *et al.* Deep Learning to Improve Breast Cancer Detection on Screening Mammography. *Sci Rep* 9, 12495 (2019). https://doi.org/10.1038/s41598-019-48995-4 [3] https://www.rcr.ac.uk/posts/rcr-position-statement-artificial-intelligence. [4] Tosaka A, Ohya K, Yamada K, et al. Incidence and properties of renal masses and asymptomatic renal cell carcinoma detected by abdominal ultrasonography. *J Urol*. 1990;144(5):1097-1099. doi:10.1016/s0022-5347(17)39667-2 [5] https://ncita.org.uk [6] O'Connor SD, Silverman SG, Cochon LR, Khorasani RK. Renal cancer at unenhanced CT: imaging features, detection rates, and outcomes. *Abdom Radiol (NY)*. 2018;43(7):1756-1763. doi:10.1007/s00261-017-1376-0 [7] Gillies, R.J., Kinahan, P.E., Hricak, H. (2015) Radiomics: images are more than pictures, they are data. Radiology, 278(2), 563-577. DOI: 10.1148/radiol.2015151169 [8] Sala, E., Mema, E., Himoto, Y., et al. (2017) Unravelling tumour heterogeneity using next-generation imaging: radiomics, radiogenomics, and habitat imaging. Clinical Radiology, 72(1), 3-10. DOI: 10.1016/j.crad.2016.09.013 [9] Liu L., et al. A survey on U-shaped networks in medical image segmentations. Neurocomputing, 409, 244-258 (2020) https://doi.org/10.1016/j.neucom.2020.05.070