Project Details	
Project Code	MRC21PHCa Beltrachini
Title	Statistical characterisation of prostatic tissue and its application to non-invasive estimation of Gleason scores
Research Theme	Population Health
Summary	Prostate cancer is the UK's most prevalent male cancer. Accurate diagnosis requires invasive biopsy for histological microscopic characterisation. While MRI-based approaches can capture some cell properties, they cannot predict histological morphology, critical to diagnosis/prognosis. This PhD project will use an extremely powerful MRI scanner and develop and test innovative statistical models to characterise prostate microstructure non-invasively as never before.
Description	Accurate diagnosis and risk stratification are crucial for optimising prostate cancer treatment. The Gleason grading system is used widely to classify the tumour's predicted behaviour, with a higher Gleason score (GS) indicating the likelihood of more aggressive disease. GSs are assigned by analysing histopathological samples and are highly dependent on the morphological arrangement of tissue components (e.g., stroma, epithelium, lumen). However, biopsies are painful and stressful for patients, are associated with infections and sepsis, and run the risk of false-negatives (due to limited sampling). Thus, there is a growing need to develop non-invasive methods to estimate GSs accurately. MRI has become a standard tool for analysing prostatic tissue. State-of-the-art methods depend on mathematical formulae linking MRI signals to microstructural features, e.g. cell radii/density. However, such formulae require simplifications to make them mathematically tractable, such as assuming tissue components are spheroidal. This has led to results that only resemble GSs phenomenologically. This PhD studentship will tackle this problem by developing a statistical framework that allows reconstruction of tissue microstructure from MRI measurements without imposing limiting models. Unlike any other existing methodology, it will result in the generation of histology-like images containing similar information to that available in real histological data from a statistical standpoint. This will be done by employing the MRI scanner to measure a series of statistical descriptors (SDs) encoding the relative arrangements and shapes of different tissue components. The use of SDs for microstructure characterisation has been previously used for non-destructive analysis of composites with scattered radiation (Torquato (2002) "Statistical description of microstructures", Annu Rev Mater Res 32:77-111) but has not yet been explored for describing biological tissue with MRI. The acquisition of SDs will be based on different properties that are known to impact the MRI signal, such as diffusivities, relaxations, and magnetic susceptibilities. Once such descriptors are obtained, they will be used to generate statistically accurate and histology-like tissue reconstructions, which can then be used to calculate GSs estimates non-invasively. The proposed methodologies will be continuously tested in simulated and real scenarios. The first will include the utilisation of computational substrates and in silico measurements in which the ground truth is known. These studies will allow to validate and refine models in developmental stages, which will be subsequently used to characterise

	prostatic tissue in real cases. Experimental validation with real data will consist of scanning real samples before extraction/fixation and comparing the results with histological outcomes and corresponding GSs. These samples will be provided through collaboration with the University Hospital Wales. The project offers training and research in a hugely interdisciplinary area, requiring the development of skills ranging from coding and mathematical modelling [including machine learning (ML) to link tissue reconstructions to GSs], to histological understanding of prostate tissue in health and disease. The candidate will therefore develop key skills in a research area sitting at the intersection of engineering, physics, and medicine to address a challenging and pressing societal problem whose solution would aid millions of people and save public funds. Timeline: During the first 6 months, the student will focus on understanding the problem, and getting insights in the areas of microstructural imaging and prostate cancer. They will will follow a course in ML that will provide a unique perspective into the problem. The next 12 months will be spent designing, optimising and test the model in simulated data. In vivo experiments and histological validation will take place largely in year 3.
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