Purpose: We describe a novel approach to treatment planning for focal brachytherapy utilizing a biologically based inverse optimization algorithm and biological imaging to target an ablative dose at known regions of significant tumor burden and a lower, therapeutic dose to low risk regions.

Materials and Methods: To demonstrate how tumor characteristics may be extracted from multi-parametric MRI (mp-MRI) to inform the previously validated biological model (1), 10 patients underwent in-vivo mp-MRI prior to radical prostatectomy. The surgical specimens were imaged to aid registration with histology which provides ground-truth data for correlation with in-vivo mp-MRI. Co-registration of histology and imaging data using rigid and deformable registration was validated by matching feature points and annotated zonal regions. Automated methods for defining tumor location, tumor cell density and Gleason Score in histology have been developed to register with mp-MRI(2,3).

Treatment plans for ten patients treated with a conventional LDR brachytherapy approach were compared with plans created with a biologically based inverse optimization planning process using a non-uniform distribution of tumor cell densities. The iterative local search approach increases the TCP to a target value whilst constraining the dose to the urethra below user defined dose/volume constraints.

Results: Co-registration of the in-vivo mp-MRI with ex-vivo MRI is challenging with considerable effort needed in image acquisition and post processing to obtain the accuracy required for focal planning (Fig 1). An ensemble-based supervised classification algorithm, trained on textural image features, demonstrates a highly sensitive method for automated tumour delineation in high resolution histology images (2). Colour deconvolution and the use of a radial symmetry transform provides measures of cell density, shown to highly correlate with expert pathologist markup of tumour location(3). Statistical methods including machine learning techniques available in R software and MATLAB have demonstrated the potential for parameter maps from mp-MRI, including ADC maps, Ktrans, and T2* to be correlated with tumour characteristics including tumour cell density, Gleason score and hypoxia.

The biological inverse optimization algorithm demonstrated significant reduction in urethral doses compared with conventional treatment approaches whilst maintaining tumor control probability (TCP) with the degree of dose reduction depending on the specified planning objectives. These plans have demonstrated robustness in the presence of clinically realistic seed displacements.

Conclusions: We present a novel approach to focal brachytherapy planning with a goal to maintain high tumour control rates with minimal toxicity.