

Patient-specific forecasting of prostate cancer growth during active surveillance using an imaging-informed mechanistic model

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ABSTRACT

Active surveillance (AS) is a suitable management option for many newly-diagnosed prostate cancer (PCa) cases, which usually exhibit low to intermediate clinical risk. In AS, patients are closely monitored *via* multiparametric magnetic resonance imaging (mpMRI), prostate-specific antigen tests, and biopsies until these reveal an increase in PCa risk that warrants treatment. Thus, AS can contribute to reduce the current overtreatment of PCa and avoid treatment side-effects that may adversely impact patients' lives without necessarily improving their longevity. However, current AS protocols rely on assessing PCa according to population-based studies, which complicates the design of personalized monitoring plans and the early detection of tumor progression. To address these issues, we propose to predict PCa growth using patient-specific forecasts based on an mpMRI-informed mechanistic model.

Here, we present a preliminary study in a cohort of seven PCa patients who enrolled in AS and had three mpMRI scans over a period of 1.4 to 4.9 years. Our mechanistic model describes PCa growth in terms of tumor cell density dynamics, consisting of mobility and proliferation modeled *via* a diffusion process and a logistic law, respectively. We segment each patient's prostate geometry on T2-weighted images and estimate tumor cell density from standard apparent diffusion coefficient (ADC) maps. To facilitate PCa modeling, we co-register each patient's mpMRI datasets with a biomechanical elastic method that aligns the prostate segmentations across the imaging datasets. The model is initialized with the data from the first mpMRI scan. Model calibration relies on a nonlinear least-squares algorithm that minimizes the mismatch between ADC-measured and model-predicted tumor cell density at the second mpMRI date. For validation, we initialize the patient-specific calibrated model with the second mpMRI dataset and forecast PCa growth at the third mpMRI date, which we compare to the corresponding ADC-estimated tumor cell density.

Model calibration resulted in a concordance correlation coefficient (CCC) ≥ 0.99 for both tumor volume and global tumor cell count across the cohort. For each patient, the spatial fit of tumor cell density at the second scan date rendered a median Dice score and CCC of 0.79 and 0.52, respectively. Model validation resulted in CCCs of 0.88 and 0.81 for tumor volume and global tumor cell count across the cohort. Comparing the patient-specific ADC-estimated and model forecasts of tumor cell density at the third scan date, we obtained a median Dice score and CCC of 0.65 and 0.46, respectively. Thus, while improvement and further testing in larger cohorts are still needed, these results do suggest that our computational forecasting approach is a promising technology to predict the spatiotemporal growth of PCa during AS on a patient-specific basis.