

Radiological and histological evolution of prostate cancer during active surveillance

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Background: Active surveillance provides a unique opportunity to observe untreated prostate cancer longitudinally. We investigated whether serial quantitative MRI captures biologically meaningful evolution of early prostate cancer and whether this information predicts subsequent histology beyond conventional radiological assessment.

Methods: We analysed 420 men undergoing active surveillance, contributing 1,603 serial MRI examinations. Longitudinal trajectories of T2-weighted lesion volume, PSA density (PSAD) and normalised apparent diffusion coefficient (ADC) were modelled jointly according to baseline Gleason grade. An independent histologically characterised PROMIS cohort (n=193) was used to relate these quantitative MRI phenotypes to prespecified definitions of clinically significant cancer ($\geq$ Def2 and Def1). MRI-derived histological risk was then compared with directly observed surveillance biopsy findings and PRECISE assessment.

Results: Over five years, MRI-visible lesions demonstrated coordinated phenotypic evolution, with approximately 58% increase in lesion volume, 13-14% increase in PSAD and 8% reduction in normalised ADC. Longitudinal rates of lesion volume and PSAD change were positively correlated ($r=0.48$, 95% CrI 0.10-0.77), supporting an evolving multivariate MRI phenotype. In men with baseline Gleason 3+3 disease, MRI-implied $\geq$ Def2 probability increased from 45.2% to 60.7% and Def1 probability from 22.3% to 32.2%. Direct surveillance biopsies showed concordant histological evolution, with increasingly adverse $\geq$ Def2 and Def1 findings and increasing maximum cancer core length over time. Among 383 MRI-biopsy pairs from 281 men, each 10-percentage-point increase in MRI-derived risk was associated with 20% greater odds of the corresponding subsequent biopsy endpoint ($\geq$ Def2: OR 1.20, 95% CI 1.11-1.29; Def1: OR 1.20, 95% CI 1.12-1.30), with AUCs of 0.642 and 0.643, respectively. PRECISE showed stronger discrimination, particularly for $\geq$ Def2, but qMRI-derived risk remained independently associated with both histological endpoints after adjustment for PRECISE, indicating complementary information.

Conclusions: Untreated prostate cancer demonstrates measurable radiological evolution during active surveillance, characterised by increasing lesion volume and PSAD and declining ADC. These changes correspond to progressively adverse histological phenotypes and subsequent biopsy findings, while providing information complementary to PRECISE. Serial quantitative MRI may therefore provide a continuous, biologically interpretable measure of tumour evolution during surveillance.

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