Reliable Prostate Cancer Risk Mapping from MRI Using Targeted and Systematic Core Needle Biopsy Histopathology

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Introduction and overall goal: Whole-gland prostate cancer (PCa) risk mapping post-biopsy can allow clinicians to better stage and personalize focal therapy treatment plans. However, the sparse ground-truth provided by the limited sample of biopsy specimens makes it difficult to assess mapping reliability in non-biopsied prostate regions. This study aims to compute a dense prostate cancer risk map for the post-biopsy individual patient from magnetic resonance imaging (MRI) and to provide a more reliable evaluation of its fitness in prostate regions that were not identified as suspicious for cancer by a human-reader in pre- and intra-biopsy image analysis.

Specific aims: To assess the predictive power of machine learning (ML) in mapping pre-biopsy imaging to histopathology in non-targeted prostate regions, while focusing on three aspects of model reliability which have been overlooked in previous studies: (i) representativeness of the biopsy validation data; (ii) whole-gland risk extrapolation using patient's post-biopsy data; (iii) quantification of model fitness at the individual patient level.

Rationale and background: Multiple attempts have been made to learn the mapping function from pre- and intra-biopsy MRI voxels to post-biopsy pathology using ML; nonetheless, these studies: (i) focused on predicting pathology in targeted-biopsy locations although biopsy specimens drawn systematically from scattered locations across the prostate constitute a more representative sample to non-biopsied regions, and (ii) estimated prediction power across predicted instances (e.g., biopsy specimens) with no patient distinction, which may be biased due to variation between patients in instance count, imaging characteristics, targeting inaccuracies and pathologies.

Methods and materials: We explored a large publicly available dataset of 962 tracked biopsy sessions held in the University of California, Los Angeles between 2004-2011, with 14,197 biopsy cores annotated with histopathology scores on pre-biopsy MRI. Pre-biopsy MRI biomarkers from targeted and non-targeted biopsy locations were extracted and statistically tested for representativeness against biomarkers from non-biopsied prostate regions. A probabilistic machine learning classifier was optimized to map biomarkers to their core-level pathology, followed by extrapolation of pathology scores to non-biopsied prostate regions. Goodness-of-fit was assessed at targeted and non-targeted biopsy locations for the post-biopsy individual patient.

Results: Our experiments showed high predictability of imaging biomarkers in differentiating histopathology scores in thousands of non-targeted core-biopsy locations (ROC-AUCs: 0.85-0.88), but also high variability between patients (Median ROC-AUC [IQR]: 0.81-0.89 [0.29-0.40]).

Discussion and conclusion: The sparseness of prostate biopsy data makes the validation of a whole gland risk mapping a non-trivial task. The focus of previous studies on targeted-biopsy locations and their use of cohort-level evaluation, may result in an unreliable estimate of model fitness to the individual patient. This study proposes a personalized whole-gland PCa risk mapping (Fig. 1) post-biopsy to provide clinicians with a valuable continuous localization of cancer across the prostate gland to further personalize their post-biopsy treatment plan.

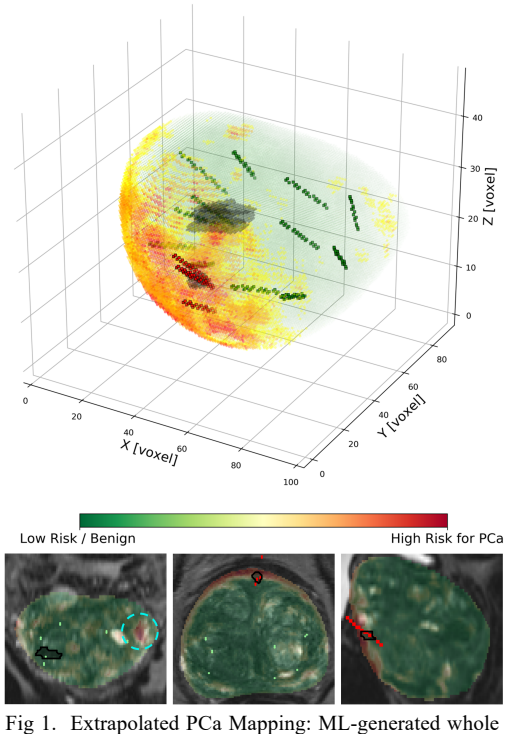

Fig 1. Extrapolated PCa Mapping: ML-generated whole prostate risk assessment for identifying PCa in 3D (top subfigure) and three 2D orientations (bottom subfigures). Green and red shading indicates low and high risk respectively. Also illustrated are the interpolated biopsy needle paths colored by pathology score: benign (green), GG≥2 (red), and pre-biopsy identified lesions (dark gray). Bounded by a light blue circle on the left-bottom subplot is a high-risk region with no previous clinical indication.