

Predicting Prostate Cancer Luminal and Basal Subtypes from Routine Biopsy Images Using Artificial Intelligence

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Background: Molecular subtyping of prostate cancer using the PAM50 and Prostate Subtyping Classifier (PSC) systems can help guide treatment decisions, but currently requires specialized genomic testing that is costly, and not widely available. Artificial intelligence applied to standard biopsy images may offer a faster, more accessible way to identify a tumor's molecular subtype directly from routine pathology slides.

Methods: We developed a deep learning model that analyzes digital images of prostate biopsies to predict PAM50 and PSC molecular subtypes, built by fine-tuning a pathology-specific artificial intelligence model on tumor images. A cohort of 903 biopsy slides from 424 patients with matched genomic testing results was used to train, validate, and test the model. Computational analysis of the tissue regions the model relied on for its predictions was reviewed by a genitourinary pathologist to describe the visual patterns linked to each molecular subtype. The model's predictions were then evaluated for their relationship to hormone therapy response in an independent clinical cohort of 131 patients and to adverse findings at surgery in 122 patients who had transitioned from active surveillance to radical prostatectomy.

Results: The model accurately predicted molecular subtype directly from biopsy images, correctly classifying PAM50 and PSC subtypes with high accuracy (AUC 0.863 and 0.81, respectively). The tissue regions the model relied on corresponded to recognizable patterns on pathology review: basal and neuroendocrine-associated tumors showed poorly formed, higher-grade glands, while luminal A and differentiated luminal tumors showed better-formed, lower-grade glands. In the treatment cohort, higher predicted luminal B scores were significantly associated with better response to hormone therapy (OR = 1.51, 95% CI: 1.07-2.12, $p = 0.01$) (**Fig. 1**). In the active surveillance cohort, higher luminal B and luminal proliferating scores were significantly associated with adverse findings at the time of surgery (OR = 2.45, 95% CI: 1.40-4.30, and OR = 2.58, 95% CI: 1.16-5.73, respectively; $p < 0.001$ and $p = 0.003$).

Conclusions: Artificial intelligence applied to routine prostate biopsy images can accurately predict molecular subtype and may help identify patients more likely to respond to hormone therapy or to have more aggressive disease at surgery. With further validation in larger, prospective, multi-institutional cohorts, this approach could provide a faster and more accessible complement to genomic testing, helping guide treatment decisions in prostate cancer.

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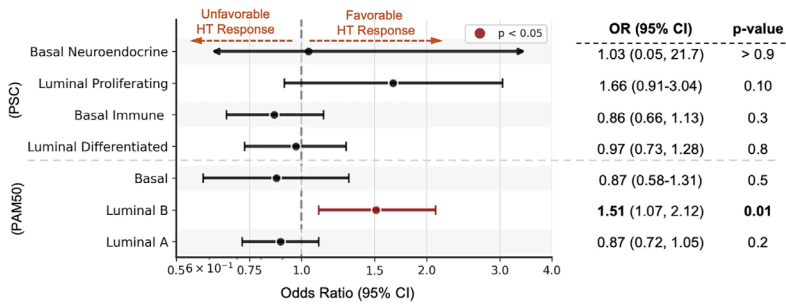


Figure 1. Forest plot showing odds ratios (ORs) and 95% confidence intervals (CIs) for each predicted molecular subtype score in predicting HT response. The PAM50 Luminal B subtype was significantly associated with a favorable HT response ($p = 0.01$)