Not in Plain Sight: Identifying Pathological Features of MRI Invisible Prostate Cancer

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Background

The utility of multiparametric MRI (mpMRI) in prostate cancer diagnosis is well demonstrated. mpMRI can prevent potentially unnecessary biopsies and target clinically significant prostate cancer (csPCa) at the time of biopsy. However, with increased mpMRI utilization, false-negative (FN) mpMRI cases are relatively common with negative predictive value ranging from 75% to 90% depending on clinical factors and radiologist variation. What drives tumor MRI invisibility at the histopathological level remains unknown. This study utilizes a deep-learning model on digital pathology to demonstrate feasibility of quantifying cellular characteristics of MRI-visible and MRI-invisible csPCa for patients with bilateral csPCa.

Methods

We performed a single institution digital pathologic analysis of H&E-stained prostate biopsy slides of patients with unilateral mpMRI lesions but subsequent bilateral csPCa on biopsy to allow patients to serve as their own internal controls. Positive biopsy blocks were categorized as MRI-visible or MRI-invisible based on laterality of the PI-RADS lesion and cores. We analyzed these biopsy blocks using CellVIT which is a deep-learning tool used to identify specific cell types on digital pathology (segmentation of cell nuclei). Four cell types were recognized: malignant neoplastic, inflammatory, connective, and prostatic epithelial cells. Cellular densities for each cell type and overall cellularity were calculated to compare MRI-visible and MRI-invisible biopsies. Two-sided Mann-Whitney tests were conducted using Python 3.10.0.

Results

We analyzed 2,152 H&E-stained digital pathology slides from 124 included patients with median age 69 years and median PSA 6.44. About 21% of patients were Black and 26% had a family history of prostate cancer. A total of 552 positive biopsy blocks were identified and analyzed. Of 198 MRI invisible blocks, 124 (63%) were Grade Group 2 (GG2), 42 (21%) GG3, 13 (6.5%) GG4, and 19 (9.5%) GG5. Of 354 MRI visible blocks, 175 (49.5%) were GG2, 85 (24%) GG3, 36 (10%) GG4, and 58 (16.5%) GG5. Cellularity was the primary differentiator between MRI-visible and MRI-invisible csPCa biopsy slides (p-value=0.0015, ROC AUC=0.6169). Neoplastic cell density was also significantly different (p-value=0.0473, ROC AUC=0.573). Differences in connective, epithelial, and inflammatory cell densities were not statistically significant.

Conclusion

Overall cellularity and neoplastic cell proportion may influence the visibility of csPCa lesions on mpMRI. Tumors with lower cellularity were more often missed suggesting differences in tissue density may impact MRI visibility (e.g. diffusion weighted imaging) or contrast characteristics. A greater proportion of blocks with MRI-invisible prostate cancer were GG2 compared to MRI-visible (63% vs. 50%). Our results

demonstrate feasibility of measuring cellular characteristics on prostate biopsy slides via digital pathology. The histopathological differences may influence the occurrence of false negative MRIs and inform when systematic biopsy may be beneficial or how to improve mpMRI imaging protocols.

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