Artificial Intelligence-based Detection of Primary Small Cell Carcinoma of Prostate

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Abstract

Background

Small cell carcinoma of prostate or neuroendocrine prostate carcinoma (NEPC) is a high grade carcinoma with aggressive disease behavior, which the diagnosis is based on characteristic histology features similar to those seen in small cell carcinoma of the lung. However, many cases of NEPC are seen admixed with conventional prostatic adenocarcinoma with a wide spectrum of morphology, leading to high diagnostic interobserver variability, which accurate diagnosis is critical for appropriate therapy. We developed a morphology-based artificial intelligence (AI) tool to assist the diagnosis of NEPC on digital whole-slide image.

Design

A deep-learning based supervised learning algorithm was trained using 73 whole slide digital images of H&E sections including prostate biopsies, transurethral resection of prostate and radical prostatectomy from patients with NEPC and Grade Group 5 conventional prostatic adenocarcinoma diagnosis to establish a dichotomous classifier (adenocarcinoma vs. NEPC). Figure 1 demonstrates supervised learning architecture for segmentation in a mixed case, which NEPC areas are denoted in yellow, and high-grade conventional adenocarcinoma areas in green. The AI classifier was further validated in two separate tissue microarrays built from 43 patients with original diagnosis of NEPC, 12 of which has concurrent admixed conventional prostatic adenocarcinoma in the diagnostic tissue blocks. The tissue microarrays were re-reviewed blindly by 2-4 uropathologists to assign the dichotomous classification per spot.

Result

After excluding tissue with extensive artifact (17 spots), a total of 165 spots representing redundant tissue microarray sampling from 43 cases were analyzed by the AI classifier and compared to pathologist consensus diagnosis for each spot by at least two uropathologists. The spots are classified as small cell carcinoma/NEPC (111 spots), high grade adenocarcinoma (44 spots), mixed adenocarcinoma and NEPC (3 spots), and 7 spots for which 4 pathologists could not reach consensus on diagnosis. The concordance rate between the AI classifier and pathologists was 75% (83/111) for NEPC and 93% (41/44) for adenocarcinoma. (**Table**)

Conclusion

As a proof-of-principle study, a morphology-based AI classifier could assist the diagnosis of NEPC with high concordance rate with uropathologists. However, the majority of the validation cases were primary NEPC with pathology consensus, and may not be representative of more challenging treatment-related NEPC. Additional studies in a treatment-related NEPC cohort are ongoing and in that setting, cases will likely require additional classification by transcriptomic data to provide ground truth classification.

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Conflicts of Interest Disclosure Statement

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Table: Validation of AI classifier in Tissue Microarray

Pathologist consensus call	All Spots number	AI agreement, spot number (%)
NEPC	111	83 (75%)
Adenocarcinoma	44	41 (93%)
Mixed NEPC+Adeno	3	2 Adeno, 1 NEPC
Tie between pathologists	7	3 Adeno, 4 NEPC
Total	165	

Figure: Supervised learning architecture for segmentation. NEPC regions are denoted in yellow, while high-grade Adeno regions are shown in green.