Deep learning models built from PSMA PET of the primary tumor can predict synchronous and metachronous prostate cancer metastases

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Background: The objective was to develop prognostic models that included convolutional neural networks (CNN) derived from ^{18}F-DCFPyL (PSMA) PET imaging of the primary tumor uptake patterns to prognose early metastatic progression after curative intent treatment for localized prostate cancer. Due to the lack of sufficient cases with adequate follow-up and metastatic events to derive this model directly, we derived models that predict the presence of synchronous metastases using only data obtained from the primary tumor. Because early metastatic progression events are consequent to occult metastases present at the time of initial therapy, we hypothesized that a model trained to predict synchronous metastases might also predict metachronous metastatic progression.

Methods: PSMA PET from 94 treatment naïve patients who underwent the scan at initial staging were used for model development. The imaging showed either unequivocal evidence for metastatic disease or no metastatic disease. The non-metastatic cases had completed curative intent therapy subsequent to the imaging and had at least 33 months of follow-up without evidence of progression from the date of the scan. aPROMISE was used to segment the entirety of the prostate and identify intraprostatic lesions while ignoring metastatic lesions. The PET images containing the entire prostate and intraprostatic lesions were inputs for the CNN. The CNN architecture was based on SqueezeNet v2. The dataset was split into training, validation and test sets using stratified random sampling. We also developed a combined multi-modal model that added conventional clinicopathologic data (PSA, pathologic grade group, percent positive cores) and measurable imaging parameters (peak SUV prostate-located value, PRIMARY score, PSMA expression score per PROMISE-V2) to the CNN via a Naïve Bayes approach.

Results: The CNN and multimodal models achieved AUCs of 0.72 and 0.82, respectively, for synchronous metastases prediction. CNN was the greatest contributing input based on Shapley additive explanation analysis. The models were applied to a cohort (n=23) who had localized disease at initial PSMA PET, underwent curative intent therapy, had at least four years follow-up, and had either no evidence of progression up to four years (n=13), or metastatic progression by PSMA PET within four years (n=10). The multimodal model discriminated between these groups with an AUC of 0.855. The CNN model alone (no contribution from clinico-pathologic or measurable imaging parameters) had an AUC of 0.727. CAPRA had an AUC of 0.768. Kaplan-Meier plots at cut points that minimize distance between ROC and point (0.1) have hazard ratio (logrank) of 0.1771 and 0.3861 for the multimodal and CAPRA models, respectively.

Conclusions: The CNN and the multimodal model trained to predict synchronous metastases also predicted metachronous metastatic progression, consistent with the notion that occult metastases present at time of initial therapy account for early metastatic progressions. Validation in a larger cohort is indicated.

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