Prognostic value of PSMA theranostic imaging in mCRPC using a fully automatic AI pipeline

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ABSTRACT

Aim/Introduction

[^{177}Lu] prostate-specific membrane antigen (PSMA) radioligand therapy (RLT) improves overall survival (OS) and progression-free survival in patients with metastatic castration-resistant prostate cancer (mCRPC). Nevertheless, early prediction of treatment response remains a major clinical challenge. This study investigates whether imaging features acquired during therapy, combined with clinical variables, can be used by artificial intelligence-based survival models to predict patient outcome.

Materials and Methods

A cohort of 46 patients with mCRPC treated with [^{177}Lu]-PSMA RLT is analysed. Lesions are segmented automatically using nnU-Net. Theranostic [^{177}Lu]-SPECT/CT scans are registered to diagnostic [^{68}Ga]-PSMA or [^{18}F]FDG PET/CT scans using rigid and ElasticSyN registrations. Lesion masks obtained on diagnostic PET/CTs are mapped onto [^{177}Lu]-SPECT/CTs, enabling longitudinal lesion assessment. For both diagnostic and theranostic scans, we calculate lesions' total volume (TV) and total activity within the prostate, lymph nodes, bones, and abdomen, segmented using TotalSegmentator, as well as whole-body TV and total lesion activity. Other clinical data such as age and prostate-specific antigen (PSA) values measured prior to theranostic cycles are also included. Survival prediction is evaluated using random survival forests (RSF). Model performances are assessed using Harrell's concordance index (C-index). To ensure robustness, we use a 5-times repeated, outer stratified 3-fold cross-validation (CV) scheme, with an inner 3-fold CV for hyperparameter optimization, and compute 95% confidence intervals (CI) for mean C-index using fold-wise bootstrapping. We consider the following endpoints: PSA progression (32 events), defined according to the PRINCE trial, as the primary endpoint; and OS (32 events) as the secondary endpoint.

Results

The nn-Unet trained and tested on Deep-PSMA, with a train/test split of 80/20%, yields a Dice Score of 0.844 (Standard deviation: 0.085). For PSA progression, mean C-index with diagnostic features alone is 0.572[95%CI: 0.568,0.576]. When concatenating diagnostic with first theranostic cycle features, C-index increases to 0.714[0.706,0.721]. When considering only theranostic features, C-index remains 0.716[0.709,0.722]. For OS, including features from the first theranostic cycle (C-index 0.584[0.576, 0.592]) shows no improvement when compared to diagnostic features alone (C-index 0.598[0.589,0.607]).

Conclusion

Despite being limited by a monocentric and small patient cohort, the integration of longitudinal imaging biomarkers and clinical variables shows potential for early outcome prediction in mCRPC patients undergoing [^{177}Lu]-PSMA RLT. Theranostic imaging achieves best prognosis predictive performance for PSA progression, whereas features from diagnostic PET/CTs do not provide further improvement. OS cannot be predicted reliably using our approach.