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AI AND DIGITAL THERAPEUTICS

1P Multimodal integration of radiology, pathology and transcriptomics for prediction of response to neoadjuvant therapy in patients with retroperitoneal liposarcoma

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Background: Retroperitoneal liposarcoma (RPLS) is defined as an aggressive malignancy for which adjuvant modalities have not shown increased efficacy compared to surgery due to its highly complex and heterogeneous features. Recent work has highlighted important prognostic information captured by computed tomography (CT) and histopathology-based multi-omics, with the potential to non-invasively characterize the so-called radiological phenotype. However, little is known about the ability to combine features from these different sources to improve the prediction of treatment response.

Methods: Eight independent cohorts of RPLS patients were enrolled from our center (n=183) and validation cohort (n=184). To develop and validate a CT-based multi-omics model to predict response to NACT (n=15) and radiotherapy (n=20) by combining contrast-enhanced CT images, genomic (n=59), bulk transcriptomic (n=100), lipidomic (n=50), plasma metabolomic (n=370), scRNA-seq (n=4) and corresponding multiplex immunohistochemistry (mIHC) (n=39) from tumor samples to assess the immune and metabolic landscape.

Results: We have developed a novel approach based on a traditional CT radiomics model to to accurately predict OS and tumor heterogeneity in RPLS. Using annotations, we developed a machine learning approach to integrate multimodal features into a risk prediction model. Our multimodal model (area under the curve (AUC) = 0.782) outperformed unimodal measures, including the clinical (AUC = 0.743), pathological (AUC = 0.723) and radiomics (AUC = 0.661). The multimodal risk score was significantly reduced with post-NACT, with more tertiary lymphoid structures (TLS) and immune cell infiltration, such as plasma cells and B cells, compared to pretreatment, and PCK1 were most significantly altered in the high multimodal risk score group with unfavourable prognosis.

Conclusions: Our study provides a quantitative rationale for using multimodal features to improve the prediction of prognosis, TIME, and response to post-NACT in patients with RPLS using expert-guided machine learning with excellent performance. This may be a promising avenue if validated by further prospective randomized trials.

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2P Using machine learning (ML) and explainable artificial intelligence (AI) to accurately predict immune-checkpoint inhibitor (ICI) response in small cell (SCLC) and non-small cell (NSCLC) lung cancer patients

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Background: ICIs are widely used in SCLC and NSCLC, however current predictors of response, such as PD-L1 expression, have limited accuracy. Until recently, identifying predictors for ICI response has been challenging. Utilising ML algorithms, we have developed models to predict ICI outcomes that can facilitate precision medicine and accelerate drug development.

Methods: 471 datasets were included for patients commencing ICIs between 2015-2024 in a U.K hospital. Chi-squared analysis was used for comparative statistics. Six ML algorithms were developed using 80% of the data for training, and 20% for validation. Shapley Additive Explanations (SHAP) explainable AI was used for model interpretation.

Results: Of the 471 patients, 431 (92%) were treated with palliative intent and 40 (8%) with curative intent. 430 (91%) had NSCLC and 41 (9%) had SCLC. Patients who had ICI after previous treatment with radiotherapy and chemotherapy had a significantly higher likelihood of progressive disease (PD) (37%) compared to patients who had ICI alone without prior radiotherapy and chemotherapy (18%) (x^2=9, p=0.003). XGBoost classifier predicted PD with 78% accuracy. Important features included increasing age, advanced TNM staging, performance status and female sex. The largest patient cohort in our dataset were 390 NSCLC patients who received treatment with palliative intent. In this cohort, the commonest ICI was pembrolizumab (302, 77%) followed by atezolizumab (62, 16%). A sub-group analysis of this cohort yielded an accuracy of 71% and found that prior radiotherapy and atezolizumab use were important features in predicting PD. Our ML algorithm predicted ICI outcomes with significantly greater accuracy (78%) than PD-L1 levels alone (21%) (x^2=298, p=0.001).

Conclusions: We developed ML algorithms that accurately predicted ICI response in patients with lung cancer. This could enable informed, shared decision-making between clinicians and patients considering initiating, continuing or stopping ICI therapies. Future work will validate the AI model by incorporating it into ICI drug development trials to prospectively predict patients' responses.

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3P Predicting immunotherapy-related adverse events in melanoma patients using machine learning algorithms and explainable artificial intelligence

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Background: Immune checkpoint inhibitor (ICI) related adverse events (irAE) can impact quality of life and necessitate the discontinuation of ICI treatment in melanoma patients. This study utilised machine learning (ML) and explainable artificial intelligence (AI) to predict irAEs in patients with melanoma as this could improve patient outcomes and support informed, shared decision-making between patients and clinicians.

Methods: 455 datasets were included for patients initiated on ICIs between 2014-2024 in a single, large regional cancer in Kent, U.K. Six ML algorithms were developed using 80% of the data for training, and 20% for validation. Shapley Additive Explanations (SHAP) explainable artificial intelligence was used to interpret the irAE prediction model to improve the interpretation and transparency of the decision boundary.

Results: Of the 455 patients, 294 patients (65%) were treated with palliative intent, while 161 (35%) were treated with curative intent. 121 patients (27%) experienced irAEs with only 29 having a documented grade of irAE (grade 1-4) whilst the remaining 92 patients had unspecified irAE grades. The commonest class of irAE (CTCAE v5) was gastrointestinal (38, 31%), followed by skin (25, 21%) and subsequently endocrine (22, 18%). Of the 121 patients with irAEs, 36 (30%) required hospital admission as a consequence of their irAEs and 49 patients (40%) stopped ICI treatment as a consequence of their irAEs. Linear Regression and Gaussian Naïve Bayes predicted irAEs with the most accuracy, 92%. The model highlighted increasing age, female gender and exposure to combination therapy or pembrolizumab as predictors for irAE.