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The Immunogradient of CD8+ cell density in the tumour-stroma interface zone predicts overall survival of patients with hormone receptor-positive invasive ductal breast carcinoma

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Statement of the Problem: Tumour infiltrating lymphocytes (TIL) are associated with better prognosis in triple-negative and HER2-positive breast cancer (1, 2), and TIL assessment by digital image analysis (DIA) has been successfully implemented in colorectal and other cancers (3). However, results in hormone receptor-positive breast cancer (HRBC) based on manual scoring remain contradictory (2). Here we used an automated DIA method to extract prognostic value of novel Immunogradient indicators in CD8+ cell density profiles in HRBC.

Methodology & Theoretical Orientation: Surgically excised HRBC samples from 102 patients were immunohistochemically stained for CD8, digitized and analysed by the HALO™ platform. The DIA data was subsampled by a hexagonal grid and explicit rules were then used to extract the tumour-stroma interface zone (IZ) and compute novel Immunogradient indicators from TIL density profiles across the IZ. The prognostic value was evaluated by survival analysis. Findings: The IZ Immunogradient indicators (mean CD8+ density in the tumour aspect of the IZ, Immunodrop, Centre of Mass) allowed prognostic stratification of patients in univariate analyses (hazard ratios: 0.21 ($p=0.0002$), 2.79 ($p=0.0140$), and 0.28 ($p=0.0044$), respectively). The best and independent indicator of better OS by multiple Cox regression model (hazard ratio: 0.23 ($p=0.0007$)) was an aggregated Immunogradient factor (Agg. Factor), obtained by the sum of two factor scores (CD8+ density and “gradient towards the tumour”). Remarkably, the aggregated Immunogradient factor revealed a striking drop of patients’ survival probability 5 years after surgery.

Conclusion & Significance: The Immunogradient indicator for CD8+ cell density is an independent predictor of better OS in HRBC patients with the particular diversion of OS 5 years after the surgery.

Biography

Dovile Zilenaite is a medical geneticist at the National Center of Pathology, Affiliate of VULSK and a doctoral student at Vilnius University Faculty of Medicine. Her research focuses on the development and standardization of multiple IHC procedures for multiparametric and spatial analysis, digital image analysis and prognostic modelling in the breast cancer patients. Main scientific interests: genetics, cancer biology, immunology, digital analysis and analytics of whole slide pathology images to describe heterogeneity of tumor cell population and microenvironment.

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