Machine and Deep Learning Approaches for Predicting VEGF Levels in Cancer Patients

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Introduction: Elevated VEGF expression in tumor microenvironment promotes tumor progression and metastasis [1]. Bevacizumab, a humanized monoclonal antibody targeting VEGF-A, is widely used alone or with chemotherapy in cancers including breast, cervical, ovarian, non-small cell lung cancer (NSCLC), and metastatic colorectal cancer (CRC) [2]. By inhibiting angiogenesis, it has shown efficacy in both frontline and recurrent settings [3].

Aims: To assess the impact of demographic factors, chemotherapy parameters, and bevacizumab levels (peak, trough, and difference [AV_D]) on VEGF levels in patients with NSCLC, CRC, breast, cervical, and ovarian cancer.

Methods: Machine learning methods and artificial neural networks (ANNs) were applied. Dimensionality reduction (CATPCA, MCA, PCA, FAMD) was used for data exploration. Predictive models (Random Forest, Boosted Trees, Bagged Trees, ANN) were developed to identify determinants of VEGF reduction (VEGF_D).

Results: CATPCA and PCA revealed opposing patterns between VEGF and bevacizumab levels, indicating distinct variance contributions. CATPCA also suggested heterogeneous VEGF reduction trajectories influenced by treatment duration and cycles. Random Forest identified AV_D, weight, and therapy cycles as key predictors, with AV_D showing the strongest dose-dependent effect. Boosted Trees and ANN confirmed AV_D as the dominant factor, while weight and treatment duration remained significant but secondary. Overall, AV_D consistently emerged as the main determinant of VEGF_D.

Conclusion: Bevacizumab-induced VEGF reduction is primarily driven by drug exposure variability rather than absolute peak or trough values. Lower AV_D, reflecting more stable exposure, enables more consistent VEGF suppression. Patient-specific factors, including weight and treatment duration, further influence outcomes, highlighting the importance of personalized therapy. Machine learning approaches proved effective in uncovering complex relationships, supporting their role in optimizing treatment strategies.

Literature:

[1] Alidzanovic L. et al. (2016) Oncotarget 7:57197–57212.

[2] EMA (2023) Avastin EPAR.

[3] Ghezelayagh T.S. et al. (2023) Eur J Gynecol Oncol 44:17–25.

Short CV:

Ileana Theofili is a PhD candidate at the Pharmacy Department of the National and Kapodistrian University of Athens, focusing on the application of artificial intelligence in pharmacotherapy. Her research explores how machine learning and deep learning models can be integrated with real-world clinical data to optimize treatment strategies, particularly in oncology. She holds an MSc in Clinical Pharmacy, a Bachelor degree in Pharmacy, and has gained clinical experience through hospital rotations in oncology, cardiology, and other medical fields. She has expertise in Python for data analysis and machine learning applications. Her current work investigates variability in drug exposure and its impact on treatment response, with an emphasis on precision medicine approaches. She aims to shape more precise and evidence-driven therapeutic strategies. In parallel, she contributes to educational initiatives that connect medicine with data science and clinical practice, while actively presenting her research at international conferences through poster and oral presentations.