

PET-based lesion graphs meet clinical data: An interpretable cross-attention framework for DLBCL treatment response prediction - *Supplementary material A*

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ABSTRACT

Diffuse Large B-cell Lymphoma (DLBCL) is a lymphatic cancer of steadily growing incidence. Its diagnostic and follow-up rely on the analysis of clinical biomarkers and 18F-Fluorodeoxyglucose (FDG)-PET/CT images. In this context, we target the problem of assisting the early identification of high-risk DLBCL patients from both images and tabular clinical data. We propose a solution based on a graph neural network model, capable of simultaneously modeling the variable number of lesions across patients, and fusing information from both data modalities and over lesions. Given the distributed nature of the DLBCL lesions, we represent the PET image of each patient as an attributed lesion graph. Such lesion-graphs keep all relevant image information, while offering a compact tradeoff between the characterization of full images and single lesions. We also design a cross-attention module to fuse the image attributes with clinical indicators, which is particularly challenging given the large difference in dimensionality and prognostic strength of each modality. To this end, we propose several cross-attention configurations, discuss the implications of each design and experimentally compare their performances. The last module fuses the updated attributes across lesions and makes a probabilistic prediction of the patient's 2-year progression-free survival (PFS). We carry out the experimental validation of our proposed framework on a prospective multicentric dataset of 545 patients. Experimental results show our framework effectively integrates the multi-lesion image information improving over a model relying only on the most prognostic clinical data. The analysis further shows the interpretable properties inherent to our graph-based design, which enables tracing the decision back to the most important lesions and features.

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Table 1

Lesions 'HeadNeck' imaging features ('FirstOrder' features in bold, 'All' features in Supp. file 'Featv4_features.csv')

Classical features	Radiomics	
Standard uptake value of the maximum intensity voxel inside the lesion (SUVmax)	Shape	Sphericity
Metabolic Tumor Volume (MTV) of the lesion	Second order	Contrast
Total lesion glycolysis (TLG) from each of the segmented lesions		Correlation
Mean intensity		Inverse difference normalized
Standard deviation of intensity		Joint energy
Entropy of intensity		

Table 2

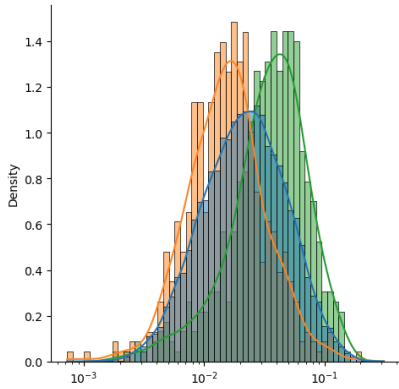
Clinical features considered in the study

Name	Explanation
Age	The higher it is, the higher the risk for the patient.
Lactate dehydrogenase (LDH)	An enzyme present in cells used as a biomarker for DLBCL diagnosis and prognosis.
Categorical LDH	Whether the LDH level is higher than it should be, the expected value depending on the measurement process.
Ann Arbor stage	Ranges from 1 to 4 depending on where the malignant tissues are located.
Number of extranodal sites	Having more than one extranodal site of involvement is usually an indication of a poor prognosis.
ECOG scale	Ranges from 0 to 5 and describes a patient's ability to take care of themselves and perform daily activities.
Age-adjusted IPI (aaIPI)	Classifies the DLBCL patients into four risk groups (0 to 3), based on 3 factors: (a) performance status - a score determining the patient's ability to perform certain day-to-day activities, (b) stage and (c) LDH level.
Treatment type	Course of treatment administered to the patient: chemotherapy regimen, autologous cell transplant or salvage therapy (which are considered as three different binary variables).

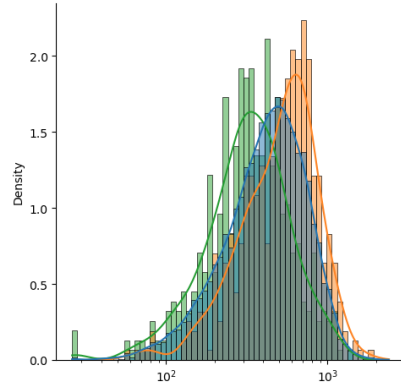
Table 3

Grid search study (HC = hidden channels ; LR = learning rate)

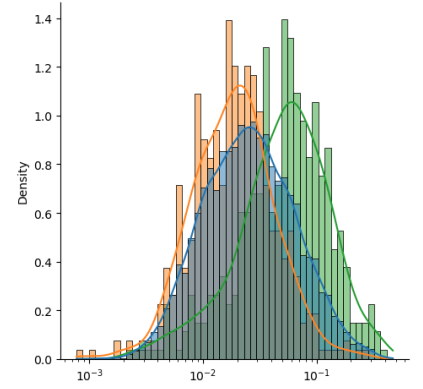
Model	Search space
MLPs	HC: {16, 32, 64, 128} LR: {0.1, 0.01, 0.001, 0.0001}
MIL	HC: {16, 32, 64, 128} LR: {0.1, 0.01, 0.001, 0.0001}
GraphConv	HC: {16, 32, 64, 128} LR: {0.01, 0.001, 0.0001, 1e-05} γ : {0.1, 1, 10, 50}
GAT	HC: {16, 32, 64, 128} LR: {0.01, 0.001, 0.0001, 1e-05} γ : {0.1, 1, 10, 50}
Cross-attention	D_{GAT} : {32, 64, 128} Dropout GAT: {0, 0.3, 0.6} Dropout cross-attention module: {0, 0.3, 0.6} LR: {0.01, 0.001, 0.0001} γ : {0.1, 1, 10, 100}
Cross-attention 2	D_{GAT} : {32, 64, 128} Dropout GAT: {0, 0.3, 0.6} Dropout cross-attention module: {0, 0.3, 0.6} LR: {0.01, 0.001, 0.0001} γ : {0.1, 1, 10, 100}
Ours (structural study)	D_{GAT} : {32, 64} D_{proj} : {16, 32, 64, 128} Dropout GAT: {0, 0.3, 0.6} Dropout cross-attention module: {0, 0.3, 0.6} LR: {0.01, 0.001, 0.0001} γ : {0.1, 1, 10}



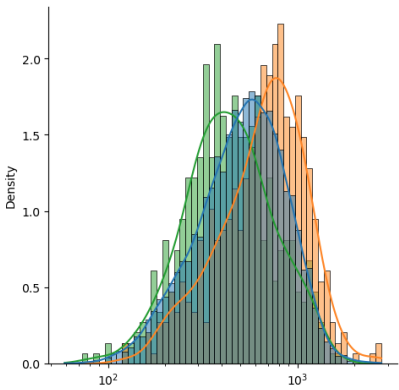
(a) original glrlm ShortRun-LowGrayLevelEmphasis BC



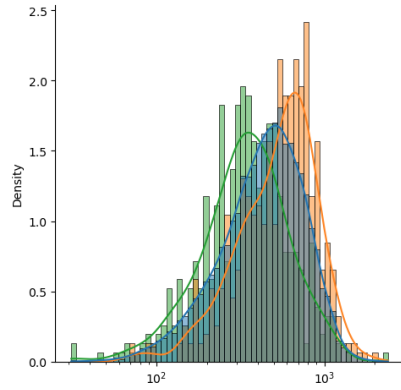
(b) original glrlm ShortRunHigh-GrayLevelEmphasis BC



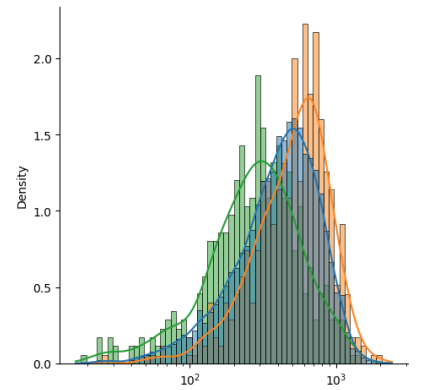
(c) original glrlm LowGrayLevelRunEmphasis BC



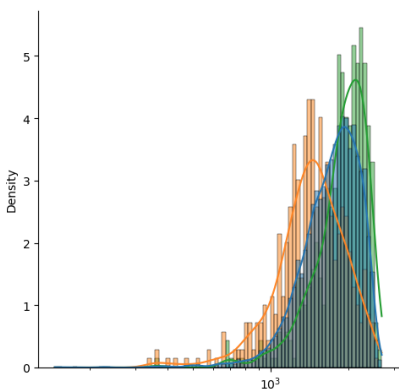
(d) original glrlm LongRunHigh-GrayLevelEmphasis BC



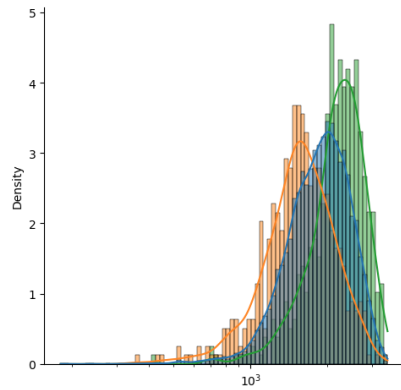
(e) original glrlm HighGrayLevelRunEmphasis BC



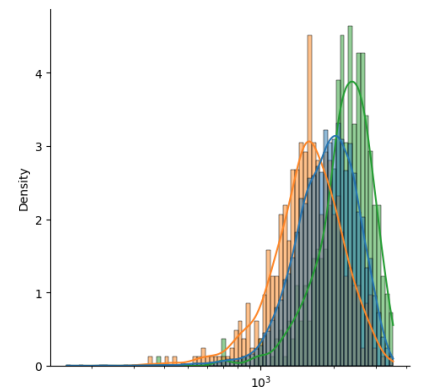
(f) original gldm HighGrayLevelEmphasis BC



(g) log sigma=6mm 3D glrlm ShortRun-HighGrayLevelEmphasis BC



(h) log sigma=6mm 3D glrlm High-GrayLevelRunEmphasis BC



(i) log sigma=6mm 3D gldm High-GrayLevelEmphasis BC

Figure 1: Imaging features for which the distribution of the retained lesions I_+ (in orange), I_- (in green) and all the lesions of the patients (in blue) are statistically different.