#3456 A highly predictive blood-radiomics classifier in advanced NSCLC treated with immunotherapy

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BACKGROUND

Untangling inter- and intra- tumor heterogeneity functional to clinical decision-making represents an unmet need of the actual Immune checkpoint inhibitors (ICIs)-driven treatment landscape. Multidimensional interrogation of circulating parameters may complement radiomics to non-invasively provide clinically suitable biomarkers.

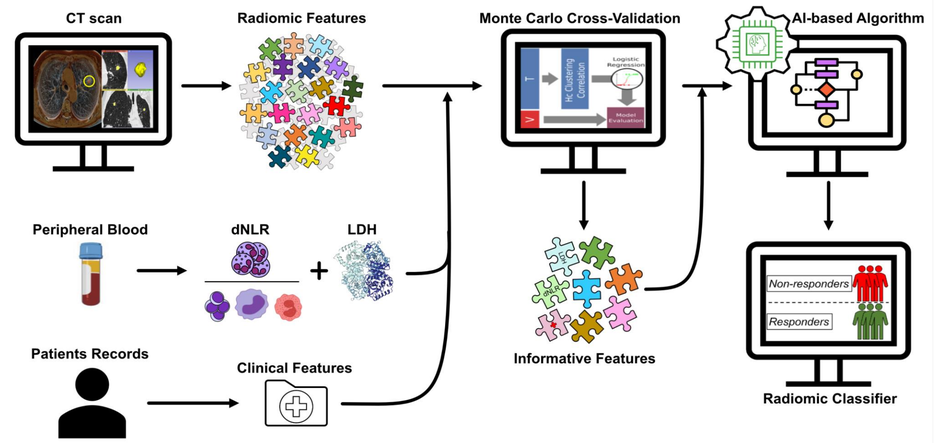
METHODS

A cohort of NSCLC patients undergoing ICIs was investigated (n=117). Baseline CT scans and peripheral blood (PB) samples served as a source of, respectively, radiomic features (RFs) and SI indices including derived Neutrophil-to-Lymphocyte ratio (dNLR) and lactate dehydrogenase (LDH). Primary endpoint was the response to ICIs per RECIST. To this end, a Monte Carlo cross-validation exploiting feature selection and logistic regression was used to uncover informative RFs. These RFs together with SI descriptors and a subset of clinical features were mined through an ad hoc genetic algorithm to maximize the classifier accuracy. The discriminative ability of the resulting top 20 selected features was assessed by Kaplan Meier and log-rank tests.

Patient Population (n = 117)		
Age, years (Median, range)		70 (41-85)
		n (%)
Sex	**Male**	80 (68)
	Female	37 (32)
Smoking status	**Smokers**	37 (31)
	Ex-Smokers	44 (38)
	Non Smokers	36 (31)
ECOG PS	**0-1**	103 (88)
	2	14 (12)
Histotype	**SCC**	35 (30)
	ADC	74 (63)
	NSCLC NOS	8 (7)
ICI Treatment	**I line**	5 (4)
	II line	100 (85)
	≥ III line	12 (11)
ICI molecule	**Nivolumab**	87 (74)
	Pembrolizumab	15 (13)
	Atezolizumab	15 (13)
Stage	**IV**	117 (100)
Metastatic Involvement	**Lymph nodes**	107 (92)
	Liver	17 (14)
	Bone	44 (38)
	Adrenal	15 (13)
	Brain	17 (14)
	Contralateral lung	112 (96)
	Pleura	36 (31)
	Others	18 (15)
Mutational status	**KRAS**	17 (14)
	EGFR	5 (4)
	ALK	2 (2)
	Others	5 (4)

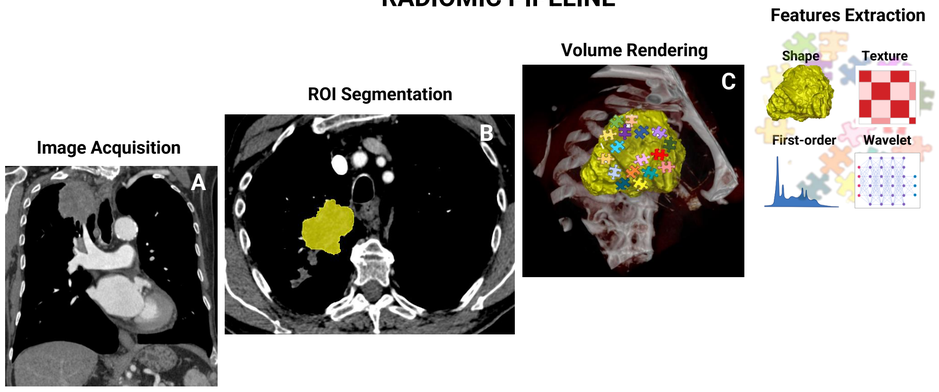
AIM OF THE STUDY

To determine whether integration of peripheral blood hallmarks of systemic inflammation (PB-SI) with high-throughput CT imaging features displays predictive power in ICI treated advanced NSCLC



Explanatory Workflow: Radiomic features (RFs, n:841) extracted from CT images together with blood descriptors of systemic inflammation (PB-SI) and clinical data were subjected to supervised multivariate analysis (Monte Carlo Cross Validation) to obtain suitable discriminatory parameters. These were processed by an Artificial Intellegence (AI) algorithm to discern the response to ICI in NCLC patients.

RADIOMIC PIPELINE



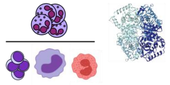
A: Coronal reformatted contrast-enhanced CT scan from a patient affected by right apical NSCLC. **B**: The corresponding axial CT scan illustrates image segmentation to draw the region of interest (ROI) highlighted in yellow. **C**: 3D reconstruction of the tumor (yellow) on which multicolor RFs are symbolically superimposed. Diagram representing the different categories of extracted RFs.

RESULTS

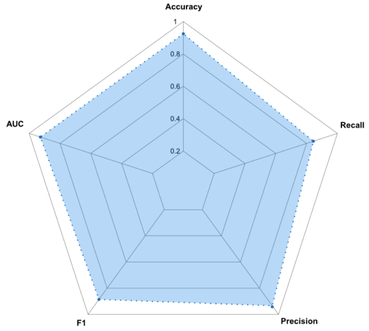
RFs

- w-hhl_glcm_idn
- w-lhl_glcm_mcc
- w-llh_glcm_imc1
- o-shape_sphericity
- w-hhl_firstorder_mean
- w-hhh_glcm_correlation
- w-lhl_glcm_clustershade
- o-firstorder_90percentile
- w-lll_firstorder_kurtosis
- w-lll_gldm_dependencevariance
- w-lll_glszm_sizezonenonuniformity
- w-hlh_glszm_smallarealowgraylevelemphasis
- w-lhh_glszm_largeareahighgraylevelemphasis
- w-lll_gldm_largedependencelowgraylevelemphasis
- w-hlh_gldm_smalldependencelowgraylevelemphasis
- w-hhl_gldm_smalldependencelowgraylevelemphasis
- w-hhl_gldm_largedependencehighgraylevelemphasis
- w-lhl_gldm_largedependencehighgraylevelemphasis

PB-SI Indices

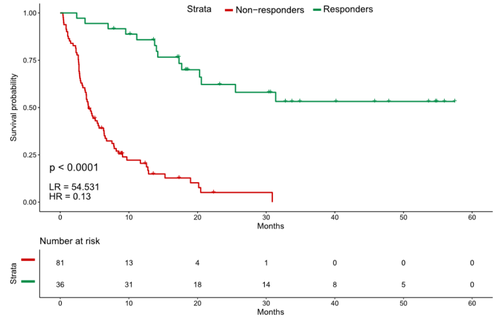


Predictive Performance



Using a leave-one-out cross-validation approach we first assessed the baseline efficiency of RFs (AUC= 0.88) and PB-SI (AUC = 0.71), respectively. When RFs (n: 18) and PB-SI (dNLR and LDH) were integrated, the resulting classifier outperformed the predictive performance of individual parameters. Radar Chart illustrates the radiomic classifier performance according to different metrics. AUC reached the highest predictive power (0.91).

Survival Analysis



Kaplan Meier curves illustrating the overall survival of NSCLC patients (N=117) sorted as non-responders and responders by our blood-radiomics classifier. Median OS was 4.1 months (95% CI, 3.6-6.4) In non-responders while was not reached in responders.

CONCLUSION

Blood-derived pro-inflammatory markers and CT-based RFs may enclose a highly predictive classifier of ICI response in NSCLC affording the non-invasive interception of tumor-immune interactions.

The present study is part of a 5-years project funded by Associazione Italiana di Ricerca sul Cancro (AIRC) gathering radiologists, pathologists, molecular biologists and oncologists to test multiomic approaches able to assess the response to immunotherapy in NSCLC.

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