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Poster

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Finding reproducible and informative radiomic features associated to clinical endpoints and to immunohistochemistry biomarkers from CT imaging data in an immunotherapy-treated NSCLC cohort

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Leyla Ebrahimpour [1, 2] , Yannick Lemaréchal [1] , Michèle Orain [2] , Fabien Lamaze [2] , Philippe Joubert [3, 2] , Philippe Despres [1, 2] , Venkata Manem [4, 2]

1. Département de physique, de génie physique et d'optique, Université Laval, Quebec City, CAN 2. Centre de recherche de l'Institut universitaire de cardiologie et de pneumologie de Québec, Université Laval, Quebec City, CAN 3. Département de biologie moléculaire, de biochimie médicale et de pathologie, Université Laval, Quebec City, CAN 4. Department of Mathematics and Computer Science, Université du Québec à Trois Rivières, Quebec City, CAN

Corresponding author: Leyla Ebrahimpour, leyla.ebrahimpour@criucpq.ulaval.ca

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Abstract

- Purpose

The objective of this study is to find reproducible and predictive radiomic features from Computed Tomography (CT) images that are correlated to clinical endpoints and immunohistochemistry (IHC) biomarkers in an immunotherapy treated non-small cell lung cancer (NSCLC) cohort.

- Materials and Methods

A retrospective study of NSCLC patients receiving immunotherapy was undertaken. The dataset includes 164 patients that have CT-scans and survival end points, while 34 of them have IHC data as well. For all of the patients, we extracted 1224 and 441 radiomics features using two IBSI-compliant pipelines, Pyradiomics and RaCat respectively. They were grouped into shape-, intensity-, and textural-based categories. The intraclass comparison between features across these two pipelines was assessed by the Pearson, Spearman, F-test, and Mutual Information estimators and corrected for false positives using the False Discovery Rate (FDR) method. To assess the influence of the clustering of pixels based on their intensity (defined as the gray-level discretization), on the robustness of features, we computed their association with two survival endpoints (Overall Survival (OS) and Progression Free Survival (PFS)) and with eight IHC markers (CD3, CD4, CD8, CD56, CD163, Lag3, PD1, and TIM) considering two different bin counts and bin width for a sub-group of 34 Samples.

- Results

Our results showed that first-order radiomic features were amongst the most reproducible features. Importantly, our findings conveyed that while the values of radiomic features were strongly pipeline-dependent, the textural radiomic features that were associated to the clinical parameters and IHC markers were strongly dependent to the type of discretization too. When changing the bin width or bin count, only 20% of the overall texture-based radiomic features have a lower rank differential change (less than 50) in the target prediction ranking score. Whereas, this value is 100% for the shape-based features and 90% for the intensity-based features.

- Conclusions

Through this work, we highlighted a significant heterogeneity between radiomic pipelines as well as the impact of gray-level discretization on the discovery of immunotherapy biomarkers in NSCLC patients. Based on this, it is crucial to standardize the radiomics processing methods to develop clinically robust predictive models in future studies.

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Leyla Ebrahimpour[1,2], Yannick Lemaréchal[1,2], Michèle Orain[2], Fabien Lamaze[2], Philippe Joubert[2,4], Philippe Després[1,2], Venkata Manem[2,3]

[1] Department of Physics, Physical Engineering, and Optics, Université Laval, Québec, Québec, Canada
[2] The Quebec Heart and Lung Institute Research Centre (CERIUSPQ), Université Laval, Québec, Québec, Canada
[3] Cancer Research Center (CRC), Université Laval, Québec, Québec, Canada
[4] Department of Molecular Biology, Medical Biochemistry and Pathology, Université Laval, Québec, Québec, Canada
[5] Department of Mathematics and Computer Science, The University of Quebec at Trois-Rivières, Trois-Rivières, Québec, Canada

OBJECTIVES

The objective of this study is to find reproducible and predictive radiomic features from Computed Tomography (CT) images by comparing two different radiomics pipelines and four different types of gray-level discretization to predict clinical endpoints and immunohistochemistry (IHC) biomarkers in an immunotherapy treated non-small cell lung cancer (NSCLC) cohort.

MATERIAL & METHODS

- We retrospectively identified 164 NSCLC patients treated with ICIs, out of which 34 of them also had IHC data.
- 1224 and 441 radiomic features from Pyradiomics and RaCat pipelines, were extracted assuming the same gray-level discretization out of which 75 features were common between the two pipelines.
- 1224 radiomic features from Pyradiomics were extracted assuming four different bin counts and bin widths.
- The extracted features from two pipelines were compared in terms of shape-, intensity-, and texture-based features using the Pearson, Spearman, and Kendall estimators.
- The impact of feature extraction pipeline and pixel clustering, based on gray-level discretization, on feature robustness was examined by evaluating the association of features with progression free survival (PFS), PD-L1 and CD8 immune counts.

RESULTS

- Features with consistent directionality between pipelines that are associated with clinical endpoints were demonstrated as potentially stable features.
- Texture-based features were found to be significantly associated with PFS.
- Pyradiomics extracted features showed more univariate statistical significance with PFS, while RaCat resulted in more significant features with PD-L1.
- By varying the gray-level discretization, the intensity-based features were found to be more stable.
- Among the 29 features that showed significant correlation with PFS considering different settings for gray-level discretization in Pyradiomics, 45% were intensity-based. Around 65% of these features were extracted using various filters on the original image.
- No particular bin size or bin count was found that led to a higher number of significant features linked to PFS, PD-L1, and CD8.

RESULTS: PIPELINE COMPARISON

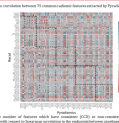

Fig 1. The correlation between 75 consensus radiomic features extracted by Pyradiomics and RaCat.

Table 1. The number of features which have strong (|CCR| or non-consistent correlation (Non-CCR) directionality with respect to Spearman correlation in the endpoints between pipelines.

Endpoint		$N_{features}$ with CCR			$N_{features}$ with Non-CCR		
		PFS	PD-L1	CD8	PFS	PD-L1	CD8
$N_{features}$		27	38	47	48	37	28
$N_{features}$ with p-value <0.05	Pyradiomics	3	0	5	24	8	0
	RaCat	1	4	0	4	2	0

Fig 2. The intersection size of the features significantly associated with PFS along with the combinations of these correlation models for Pyradiomics (**Left**) and RaCat (**right**) extracted features.

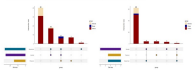

Table 2. The common features between Pyradiomics and RaCat which show statistically significant correlation with PFS.

Feature name	$P_{Spearman}$ (P-value)	
	Pyrads	RaCat
glcm_Correlation	-0.163 (0.177)	0.163 (0.238)
glcm_InverseVariance	-0.159 (0.023)	0.196 (0.047)
glszm_LargeAreaEmphasis	-0.102 (0.015)	0.182 (0.040)
glszm_LargeAreaLowGrayLevelEmphasis	-0.168 (0.016)	0.175 (0.020)
glszm_ZonePercentage	0.108 (0.045)	0.190 (0.057)
glszm_ZoneVariance	-0.161 (0.015)	0.186 (0.034)
gldm_LargeDependenceEmphasis	-0.171 (0.029)	0.145 (0.006)

Progression Free Survival; *Programmed Death-Ligand 1

RESULTS: GRAY-LEVEL DISCRETIZATION COMPARISON

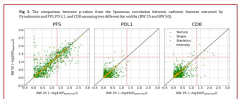

Fig. 3. The comparisons between p-values from the Spearman correlation between radiomic features extracted by Pyradiomics and PFS, PD-L1, and CD8 assuming four different bin widths (BW) (A and BW) (B).

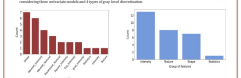

Fig 4. The frequency of significant correlated features with PFS (p-value <0.05) within each group (**left**) and sub-group (**right**) considering the same extracted models and 4 types of gray-level discretization.

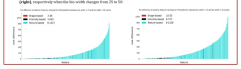

Fig 5. The ranking differences from Spearman correlations of PFS radiomics extracted radiomic features with PFS (**left**) and CD8 (**right**), respectively when the bin width changes from 25 to 50.

CONCLUSIONS

Our study has revealed a considerable degree of heterogeneity between radiomic pipelines and highlighted the importance of gray-level discretization in discovering immunotherapy biomarkers in NSCLC patients. These findings emphasize the need to standardize radiomics processing methods to improve reproducibility and reliability of radiomics analysis for developing clinically robust predictive models in NSCLC patients. Future studies could investigate how patient demographics may influence the reproducibility and predictive value of radiomic features to enhance the accuracy of predictive models.

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CONTACT INFORMATION

Email: leyla.ebrahimpour@chuljaq.ulaval.ca
LinkedIn: Leyla-ebrahimpour