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Stability of textural PET radiomics features across SUVmax-based VOI segmentation thresholds: A clinical PET/CT study

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ABSTRACT

Introduction: The stability of quantitative PET radiomics features is an important consideration for reproducible radiomics analysis. This study investigated the stability of textural PET radiomics features across different SUVmax-based VOI segmentation.

Methods: PET/CT images from 24 patients with primary colon adenocarcinoma and 24 patients with hepatic metastases were retrospectively analyzed. Lesion VOIs were automatically generated using four SUVmax-based segmentation thresholds (10%, 20%, 30%, and 40%). A total of 32

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textural features were extracted for each VOI. Feature stability was assessed using the intraclass correlation coefficient (ICC), with 95% confidence intervals.

Results: The stability of textural radiomics features varied across individual features and SUVmax-based segmentation thresholds. In the liver metastasis cohort, 28.1% of features demonstrated good to excellent stability, compared with 53.1% in the colon adenocarcinoma cohort. The feature with the highest stability was GLZLM_HGZE in the liver metastasis cohort (ICC = 0.923) and GLZLM_SZHGE in the colon adenocarcinoma cohort (ICC = 0.947). Several of the features with the highest ICC values belonged to the GLZLM and GLRLM families, whereas GLCM features generally showed lower stability, particularly in the liver metastasis cohort.

Conclusion: Textural PET radiomics features exhibit feature-dependent stability to changes in SUVmax-based VOI segmentation thresholds. The identification of features that remain stable across segmentation conditions may help improve the reproducibility of PET radiomics analyses. Differences in the observed stability patterns between colon adenocarcinoma and hepatic metastases should be interpreted cautiously because lesion size, uptake characteristics, lesion-to-background contrast, and partial-volume effects may also contribute to these differences.

Keywords: Radiomics; Positron emission tomography; Feature stability

INTRODUCTION

Positron Emission Tomography (PET) imaging plays a central role in oncology by enabling non-invasive assessment of tumor metabolism, staging, prognosis, and treatment planning [1]. Quantitative indices extracted from PET, such as the Standardized Uptake Value (SUV), have been widely used since the 1990s, and their correlation with tumor aggressiveness has been proven across various cancers [2-4]. Moreover, volumetric parameters like Metabolic Tumor Volume (MTV) and Total Lesion Glycolysis (TLG) provide additional prognostic value by integrating metabolic activity and tumor burden information [4, 5]. However, conventional PET metrics are limited in fully reflecting tumor biology, including heterogeneity, hypoxia, proliferation, and necrosis, which are determinants of clinical outcomes [4-6]. While more advanced tracers targeting specific molecular pathways are under development, there remains a parallel need to develop imaging biomarkers that more comprehensively characterize the tracer distribution and tumor phenotype.

Radiomics has emerged as a promising approach to bridge this gap. Through high-throughput extraction of quantitative imaging features, radiomics aims to non-invasively decode tumor phenotypes [7-10]. By quantifying textural, morphological, and statistical patterns from routine images, radiomics has the potential to reflect underlying tumor heterogeneity and biological aggressiveness, potentially reducing reliance on repeated invasive biopsies [11]. In PET imaging, radiomics features can capture metabolic heterogeneity and the spatial distribution pattern of the tracer, offering improved predictive and prognostic insights, particularly in the context of treatment response assessment in radiation oncology [12, 13].

However, translating radiomics findings into clinical application is hampered by concerns regarding feature robustness and reproducibility. Radiomics features are sensitive to variations in multiple factors, including image acquisition protocols, reconstruction algorithms, preprocessing, gray-level normalization, and most critically, methods for tumor delineation [13-15]. Specifically, tumor volume delineation, often performed manually or semi-automatically, introduces

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subjectivity and variability that can significantly affect feature stability [16, 17]. Variability in the size and shape of the region of interest (ROI) can cause inconsistent textural feature values, potentially undermining the validity of predictive models. Although technical sources of variability have been extensively investigated, further research is needed to fully understand how ROI size and delineation variations affect the reliability of PET radiomics features- particularly in comparative analyses involving different tumor types (primary vs. metastatic) and organs.

This study aimed to evaluate the stability of PET textural features across variations of ROI size and identify segmentation-independent features in two distinct clinical cohorts: patients with primary colon tumors and patients with liver metastases. Using intraclass correlation coefficient (ICC) analysis on four different ROI sizes for each lesion, this research sought to quantify the reliability of common textural features from various categories and provide evidence regarding whether this stability depends on the target tissue. These findings represent a step towards standardizing feature extraction and enhancing the generalizability of PET radiomics models in clinical applications.

METHODS

Data collection and preprocessing

This study was approved by the Research Ethics Committee of Tabriz University of Medical Sciences (Ethics Code: IR.TBZMED.REC.1400.800). In this retrospective study, two independent datasets of PET/CT images from patients referred to our institution were used. The liver metastasis cohort included 24 patients with biopsy-confirmed hepatic metastatic lesions, and the colon cancer cohort included 24 patients with primary colon adenocarcinoma. All images were acquired using a GE Discovery IQ PET/CT scanner and a standard protocol of 3.7 $MBq.kg^{-1}$ of [^{18}F]FDG radiotracer, with scanning performed 60 minutes post-injection. Image reconstruction was performed using the Time-of-Flight (TOF) - Ordered Subset Expectation Maximization (OSEM) algorithm. The number of subsets was 24 and the number of iterations was 4. A matrix size of 128×128 was used. Gaussian filters with a Full Width at Half Maximum (FWHM) of approximately 5 mm were applied for noise reduction.

VOI segmentation and radiomics feature extraction

For each patient, volumes of interest (VOIs) were automatically delineated on target lesions using LIFEx software (version 7.1) based on predefined percentages of SUVmax. To investigate the stability of textural radiomics features under controlled variations in VOI definition, four SUVmax-based segmentation thresholds (10%, 20%, 30%, and 40% of SUV_{max}) were applied to each lesion. These thresholds were used as controlled segmentation conditions to evaluate the sensitivity of individual radiomics features to variations in VOI delineation, rather than as independently validated clinical segmentation methods. A total of 32 textural features from four main texture-matrix families were extracted from each VOI under each segmentation condition. Textural feature categories included gray-level co-occurrence matrix (GLCM, n=7), gray level run length matrix (GLRLM, n=11), grey-level zone length matrix (GLZLM, n=11), and neighborhood grey-level difference matrix (NGLDM, n=3). A total of 32 textural features from four main texture-matrix families were extracted from each VOI under each segmentation condition. Texture feature extraction was performed using LIFEx version 7.1. The original PET voxel dimensions were 3.646 × 3.646 × 3.260 mm^3. No spatial resampling was applied, and texture features were

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calculated using the original voxel dimensions. Absolute intensity discretization was used with 64 gray levels over an SUV range of 0–20, corresponding to a fixed bin width of 0.3125 SUV. The analysis was performed in 3D with a voxel distance of 1 for neighboring-voxel calculations. For directional matrices, the LIFEx implementation uses 13 directions in 3D and averages the resulting feature values across directions. The PET intensity range and volume limits were set to 0–20 SUV and 10–1000 cm^3, respectively. No additional intensity normalization or image filtering was applied before texture extraction. IBSI-referenced feature definitions implemented in LIFEx were used where applicable.

Radiomics feature stability analysis

The stability of features against ROI size changes was assessed using the intraclass correlation coefficient (ICC (3,1)). The four predefined SUVmax-based segmentation conditions were treated as fixed measurement conditions, and the objective was to assess the stability of each feature across these predefined conditions. ICC calculation was performed using the Pingouin package in Python. A 95% confidence interval (95% CI) was also calculated for each ICC. The interpretation of ICC results was based on the following standard criteria [16]:

- Excellent (Highly Recommended): ICC > 0.9
- Good (Recommended): 0.75 < ICC ≤ 0.9
- Moderate (Conditionally Recommended): 0.5 < ICC ≤ 0.75
- Poor (Not Recommended): ICC ≤ 0.5

RESULTS

Detailed results of radiomics feature stability for all 32 evaluated textural radiomics features, including ICC estimates, 95% confidence intervals for the colon cancer and hepatic metastasis cohorts are presented in Tables 1 and 2, respectively. The stability of individual textural radiomics features varied across the evaluated SUVmax-based segmentation thresholds. Several features demonstrated high stability across the four segmentation conditions, whereas others showed greater sensitivity to changes in VOI definition. Among the 32 evaluated features one feature (3.1%) demonstrated excellent stability (ICC > 0.90), 8 features (25%) demonstrated good stability (0.75 < ICC ≤ 0.90), and the remaining features showed moderate or poor stability. The most stable feature was GLZLM_HGZE, with an ICC of 0.923 and a 95% confidence interval of [0.86–0.96]. Several of the features with the highest ICC values belonged to the GLZLM and GLRLM families. In the colon adenocarcinoma dataset 6 features (18.8%) demonstrated excellent stability, 11 features (34.4%) demonstrated good stability, and the remaining features showed moderate or poor stability. The most stable feature was GLZLM_SZHGE, with an ICC of 0.947 and a 95% confidence interval of [0.91–0.97]. The distribution of stable features differed between the two cohorts. Several of the features with the highest ICC values belonged to the GLZLM and GLRLM families. In the colon adenocarcinoma cohort, five GLCM features achieved good stability, whereas GLCM features generally showed lower stability in the liver metastasis cohort. These findings describe differences in the observed stability patterns between the two cohorts. Figure 1 presents the top 10 ICC values for the liver metastasis cohort, and Figure 2 presents the corresponding results for the colon adenocarcinoma cohort.

DISCUSSION

The main finding of this study was that the stability of textural PET radiomics features varied considerably across SUVmax-based VOI segmentation thresholds. While several features demonstrated relatively high stability across the evaluated segmentation conditions, others were substantially more sensitive to changes in VOI definition. This finding indicates that radiomics features should not be assumed to be equally robust to segmentation-related variations. Instead, feature-specific stability assessment may be an important step before using textural PET radiomics features in subsequent quantitative or predictive analyses. The present study was designed primarily to investigate whether individual textural radiomics features remain stable when the definition of the analyzed VOI is systematically altered. The four SUVmax-based thresholds (10%, 20%, 30%, and 40%) therefore served as controlled segmentation perturbations. The purpose was not to establish the superiority of one segmentation threshold or to demonstrate that one disease or tissue type inherently produces more stable radiomics features. Rather, the analysis was intended to identify features that are comparatively robust to changes in lesion delineation.

In this study, we evaluated the stability of PET textural radiomics features with respect to variations in ROI size using the intraclass correlation coefficient ICC(3,1) across two distinct clinical datasets. The findings demonstrated substantial differences in feature stability between hepatic metastatic lesions and primary colon tumors. In the liver metastasis dataset, only 28.1% of features (9 out of 32) exhibited good-to-excellent stability (ICC > 0.75), whereas in the colon cancer dataset this proportion increased to 53.1% (17 out of 32). The overall mean ICC was also higher for colon tumors (0.721) compared with liver metastases (0.619).

The stability patterns differed between the colon adenocarcinoma and hepatic metastasis cohorts. However, this finding should be interpreted as a difference in the observed feature-stability patterns rather than as evidence of intrinsic tissue-specific stability of PET radiomics features. Several lesion- and image-related factors may contribute to this observation, including lesion volume, number of sampled voxels, lesion-to-background contrast, tracer uptake, and partial-volume effects. Lesion size is particularly relevant because smaller lesions contain fewer voxels and may be more susceptible to partial-volume effects and background contamination. Furthermore, changing the SUV_{max}-based segmentation threshold modifies not only the physical extent of the VOI but potentially also the intensity distribution and the relative contribution of lesion and background activity. Consequently, differences in the observed stability patterns between the two cohorts cannot be attributed exclusively to tissue type without accounting for these factors.

Lesion heterogeneity may also influence the sensitivity of radiomics features to segmentation changes. In heterogeneous lesions, relatively small changes in VOI boundaries may modify the distribution of voxel intensities and spatial relationships within the analyzed volume, potentially affecting texture measurements. Therefore, the observed differences in feature stability between the two cohorts may partly reflect differences in lesion heterogeneity, in addition to differences in lesion size and lesion-to-background contrast. However, because heterogeneity itself was not independently controlled in the present analysis, this interpretation should be considered exploratory [18, 19]. Conversely, more homogeneous lesions tend to yield more consistent feature measurements. Partial-volume effects (PVE) may represent another source of variability, particularly when lesion dimensions approach the spatial resolution of the PET system. Under such conditions, small changes in VOI boundaries may disproportionately affect the measured activity

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distribution and the relative contribution of surrounding background activity. This effect may be particularly relevant for smaller lesions with limited voxel sampling. Accordingly, variations in VOI definition may affect intensity- and spatial-dependence-based features, including GLCM-derived features such as GLCM_Entropy and GLCM_Homogeneity [20, 21].

Features derived from the GLZLM and GLRLM matrices showed relatively higher stability for some of the evaluated features, whereas other features demonstrated greater sensitivity to changes in VOI definition. For example, GLZLM_HGZE, GLRLM_SRHGE showed comparatively high ICC values across the evaluated segmentation conditions [22]. In contrast, GLZLM_LZLGE showed greater variability. These findings suggest that sensitivity to segmentation changes may differ among individual texture features, even within different texture-matrix families. However, the present study does not establish a specific biological or mathematical mechanism underlying the higher stability of individual features [23, 24].

In the current study, four predefined SUVmax-based segmentation thresholds were applied uniformly across all lesions. Increasing the threshold progressively reduced the spatial extent of the analyzed VOI, thereby changing both the number of sampled voxels and potentially the distribution of voxel intensities within the VOI. At lower thresholds, the VOI may include more peripheral voxels and potentially a greater contribution from surrounding background activity, whereas higher thresholds may restrict the analysis to a smaller, more metabolically active portion of the lesion. These changes provide a plausible explanation for why individual radiomics features may exhibit different degrees of stability across segmentation conditions [8, 17, 25].

Overall, radiomics feature stability should be considered a feature-dependent property that can be affected by the characteristics of the analyzed lesion and by variations in VOI definition. The present findings underscore the importance of evaluating feature robustness before incorporating radiomics features into subsequent quantitative or predictive analyses. Features demonstrating high ICC values under the tested segmentation conditions may be considered comparatively stable within the specific imaging and segmentation framework evaluated in this study; however, ICC-based stability alone does not establish predictive, prognostic, or biological validity. Reporting ICC estimates together with their confidence intervals can provide a more complete assessment of feature stability. Future studies should evaluate the reproducibility of candidate features across a broader range of lesion sizes, lesion-to-background contrasts, segmentation approaches, scanners, and acquisition/reconstruction conditions.

This study has several limitations. First, the relatively small sample size in each cohort may limit the generalizability of the findings, and larger multicenter studies are needed for validation. Second, all PET/CT examinations were acquired using a single scanner and a fixed acquisition and reconstruction protocol, limiting the assessment of inter-scanner and protocol-related variability. Third, VOIs were defined using predefined SUVmax-based thresholds (10%, 20%, 30%, and 40%), which represent controlled segmentation conditions but do not encompass the variability associated with other segmentation approaches. Changes in these thresholds also affect VOI extent, voxel number, and potentially the intensity distribution. In addition, lesion-related factors such as lesion volume, lesion-to-background contrast, and partial-volume effects were not independently controlled and may have contributed to the observed stability patterns. Finally, the analysis was limited to 32 textural features; therefore, the findings cannot be generalized to first-order or shape-based radiomics features.

CONCLUSIONS

This study shows that the stability of PET radiomics features vary across individual features under different SUVmax-based VOI segmentation thresholds. Some textural features showed relatively high stability, whereas others were more sensitive to changes in VOI definition. Stability patterns also differed between the primary colon adenocarcinoma and hepatic metastasis cohorts; however, these differences should be interpreted cautiously because lesion-related factors such as volume, voxel sampling, lesion-to-background contrast, and partial-volume effects were not independently controlled. Overall, the findings highlight the importance of feature-specific stability assessment before incorporating PET radiomics features into subsequent quantitative or predictive analyses. Further validation in larger, multicenter datasets and under different imaging and segmentation conditions is warranted.

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Table 1. Stability of textural PET radiomics features across SUVmax-based VOI segmentation thresholds in patients with colon cancer

Colon cancer subjects				
Feature	**ICC (3,1)**	**95% CI_Lower**	**95% CI_Upper**	**ICC_Interpretation**
GLZLM_SZHGE	0.947	0.91	0.97	Excellent
GLRLM_SRHGE	0.937	0.88	0.97	Excellent
GLRLM_LRLGE	0.934	0.88	0.97	Excellent
GLZLM_HGZE	0.930	0.88	0.97	Excellent
GLRLM_HGRE	0.930	0.87	0.97	Excellent
GLZLM_ZP	0.903	0.83	0.95	Excellent
GLZLM_LGZE	0.890	0.81	0.94	Good
GLZLM_SZE	0.869	0.77	0.93	Good
GLRLM_LGRE	0.862	0.76	0.93	Good
GLCM_Dissimilarity	0.850	0.74	0.92	Good
GLRLM_SRE	0.804	0.67	0.90	Good
GLCM_Entropy_log10	0.797	0.67	0.89	Good
GLCM_Entropy_log2[=JointEntropy]	0.797	0.67	0.89	Good
GLRLM_SRLGE	0.786	0.64	0.89	Good
GLCM_Homogeneity[=InverseDifference]	0.785	0.65	0.89	Good
GLCM_Contrast[=Variance]	0.770	0.63	0.88	Good
GLZLM_SZLGE	0.753	0.60	0.87	Good
GLZLM_LZHGE	0.747	0.60	0.87	Moderate
GLCM_Correlation	0.704	0.54	0.84	Moderate
GLRLM_GLNU	0.683	0.50	0.84	Moderate
GLZLM_GLNU	0.664	0.49	0.82	Moderate
NGLDM_Busyness	0.658	0.48	0.81	Moderate
GLRLM_RP	0.650	0.47	0.81	Moderate
GLRLM_RLNU	0.634	0.43	0.81	Moderate
GLZLM_LZE	0.620	0.43	0.79	Moderate
NGLDM_Contrast	0.603	0.41	0.78	Moderate
GLZLM_ZLNU	0.593	0.40	0.77	Moderate
NGLDM_Coarseness	0.509	0.31	0.71	Moderate
GLZLM_LZLGE	0.476	0.27	0.69	Poor
GLRLM_LRHGE	0.450	0.23	0.68	Poor
GLRLM_LRE	0.424	0.20	0.66	Poor
GLCM_Energy[=AngularSecondMoment]	0.099	0.00	0.34	Poor

ICC: Intraclass correlation coefficient

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Table 2. Stability of textural PET radiomics features across SUVmax-based VOI segmentation thresholds in patients with liver metastases

Hepatic metastasis lesion subjects				
Feature	**ICC (3,1)**	**95% CI_Lower**	**95% CI_Upper**	**ICC_Interpretation**
GLZLM_HGZE	0.923	0.86	0.96	Excellent
GLRLM_HGRE	0.898	0.82	0.95	Good
GLZLM_SZHGE	0.892	0.81	0.95	Good
GLRLM_SRHGE	0.891	0.81	0.95	Good
GLZLM_LGZE	0.857	0.76	0.93	Good
GLRLM_LGRE	0.85	0.74	0.93	Good
NGLDM_Busyness	0.833	0.72	0.91	Good
GLZLM_SZE	0.83	0.72	0.91	Good
GLRLM_SRLGE	0.823	0.7	0.91	Good
NGLDM_Coarseness	0.746	0.59	0.87	Moderate
GLZLM_GLNU	0.738	0.58	0.86	Moderate
GLZLM_SZLGE	0.701	0.53	0.84	Moderate
GLRLM_GLNU	0.689	0.51	0.83	Moderate
GLRLM_RP	0.658	0.48	0.81	Moderate
GLCM_Energy[=AngularSecondMoment]	0.586	0.39	0.76	Moderate
GLRLM_LRHGE	0.565	0.36	0.75	Moderate
GLCM_Correlation	0.564	0.37	0.75	Moderate
GLRLM_LRLGE	0.56	0.36	0.75	Moderate
GLRLM_LRE	0.546	0.34	0.74	Moderate
GLZLM_ZP	0.543	0.34	0.73	Moderate
GLCM_Contrast[=Variance]	0.529	0.33	0.72	Moderate
GLRLM_RLNU	0.5	0.29	0.71	Moderate
GLZLM_ZLNU	0.487	0.28	0.69	Poor
GLCM_Entropy_log10	0.48	0.28	0.69	Poor
GLCM_Entropy_log2[=JointEntropy]	0.48	0.28	0.69	Poor
GLCM_Homogeneity[=InverseDifference]	0.456	0.25	0.67	Poor
GLZLM_LZE	0.433	0.23	0.65	Poor
NGLDM_Contrast	0.392	0.19	0.62	Poor
GLRLM_SRE	0.361	0.15	0.6	Poor
GLZLM_LZHGE	0.342	0.14	0.58	Poor
GLCM_Dissimilarity	0.335	0.13	0.57	Poor
GLZLM_LZLGE	0.325	0.12	0.56	Poor

ICC: Intraclass correlation coefficient

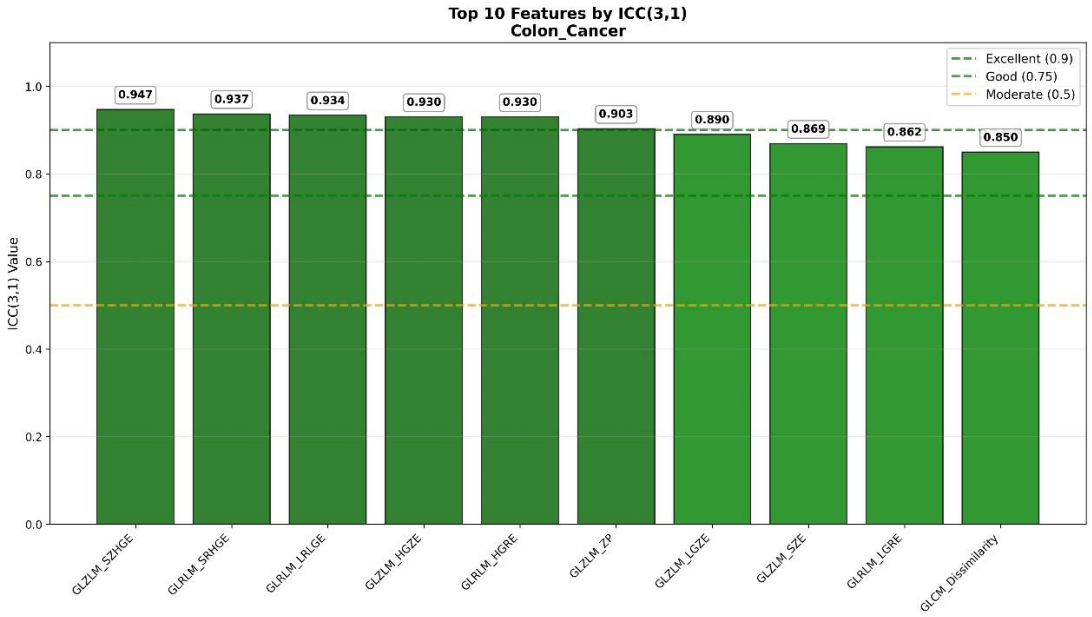


Figure 1. Top 10 intraclass correlation coefficient (ICC) values for the colon cancer dataset

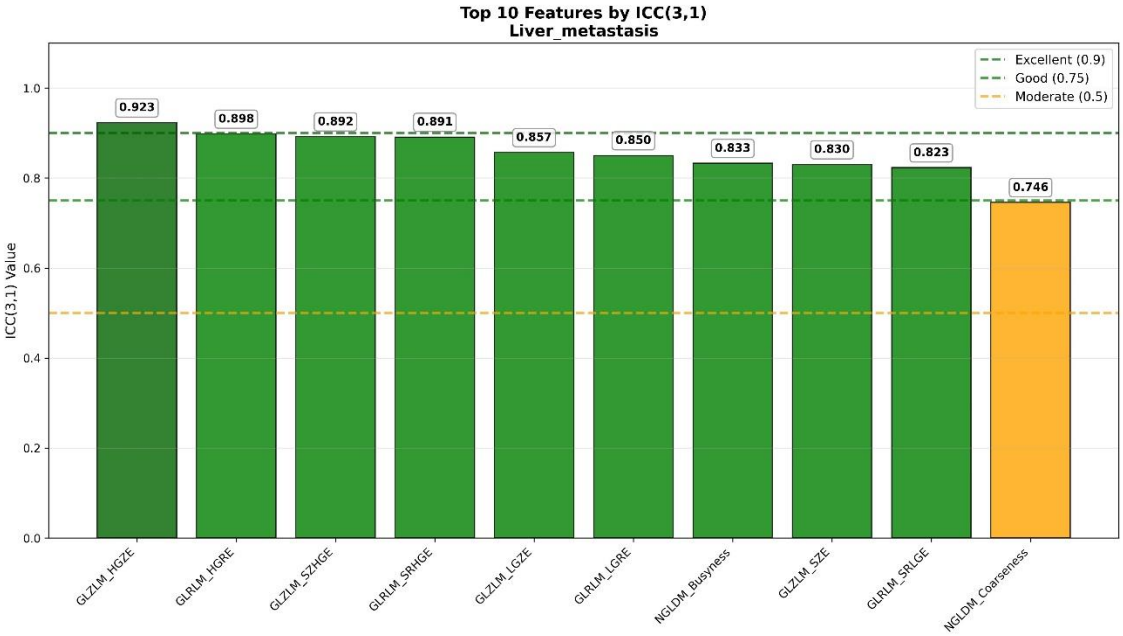


Figure 2. Top 10 intraclass correlation coefficient (ICC) values for the hepatic metastasis dataset