

Supplementary Materials

CT-based radiomics analysis to predict malignancy in patients with intraductal papillary mucinous neoplasm (IPMN) of the pancreas

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Table 1. Detailed patients' characteristics in the training and validation cohort.

Branch Duct-IPMN	Training cohort (101)		Testing cohort (32)		<i>p</i>
Category	Benign (72) (71%)	Malignant (29) (29%)	Benign (19) (59%)	Malignant (13) (41%)	0.22
Age (mean, range)	58.6 (30-82)	62.8 (42-74)	58.5 (38-74)	65.8 (55-75)	0.20
Gender					0.41
Male	32 (44%)	20 (69%)	11 (58%)	8 (62%)	
Female	40 (56%)	9 (31%)	8 (42%)	5 (38%)	
Surgical indications					
Clinical features					
Jaundice	0 (0%)	1 (3%)	1 (5%)	2 (15%)	0.02
Acute pancreatitis	34 (47%)	9 (31%)	9 (47%)	2 (15%)	0.41
Laboratory tests					
Elevation of CA 19-9	2 (3%)	0 (0%)	0 (0%)	0 (0%)	0.42
Radiological features					
WF / HRS	24 (33%)	19 (66%)	9 (47%)	9 (69%)	0.18
Others*	40 (56%)	7 (24%)	23 (121%)	7 (54%)	2.4x10 ⁻⁶
CECT phase					
Pancreatic phase	63 (88%)	27 (93%)	16 (84%)	7 (54%)	0.02
Portal phase	9 (13%)	2 (7%)	3 (16%)	6 (46%)	
Days between CECT and surgical resection (mean, range)	64.7 (1-180)	51.3 (1-132)	96.3 (5-180)	70.3 (12-139)	0.01
Type of surgery					
Duodenopancreatectomy	32 (44%)	17 (59%)	7 (37%)	8 (62%)	0.86
Left pancreatectomy	10 (14%)	2 (7%)	2 (11%)	3 (23%)	
Others	29 (40%)	10 (34%)	12 (63%)	2 (15%)	
Grade dysplasia					
	Low grade (72)	High grade (22) Invasive (7)	Low grade (19)	High grade (7) Invasive (6)	0.14
Phenotype classification (from 2012)					
Gastric	23 (32%)	6 (21%)	7 (37%)	3 (23%)	0.93
Intestinal	7 (10%)	2 (7%)	4 (21%)	0 (0%)	
Pancreatobiliary	1 (1%)	11 (38%)	0 (0%)	4 (31%)	
Oncocytic	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
Lymphadenopathy on specimen	0 (0%)	2 (7%)	0 (0%)	1 (8%)	0.70

¹Abdominal pain, weight loss, diabetes, exocrine insufficiency, familial history of pancreatic cancer, totalization after high-grade dysplasia on the first specimen, abnormal blood liver tests.

IPMN: Intraductal papillary mucinous neoplasms; CA 19.9: cancer antigen 19.9; CECT: contrast-enhanced CT; WF: worrisome findings; HRS: high risk stigmata

Table 2. Complementary subset of radiomic features in the training cohort and the external validation cohort presenting statistically significant differences between benign and malignant groups. The adjusted p-value, AUC, optimal cut-off, accuracy, sensitivity, and specificity are provided for the training cohort.

Features	Training Cohort						External Validation Test Cohort		
	p-value adj.	AUC	Cutt-off	Accuracy	Sensitivity	Specificity	Accuracy	Sensitivity	Specificity
firstorder_Energy	0.00	0.75	19284480.50	0.69	0.65	0.74	0.58	0.48	0.70
firstorder_TotalEnergy	0.00	0.75	24105600.63	0.69	0.65	0.74	0.62	0.47	0.81
gldm_SmallDependenceLowGrayLevelEmphasis	0.00	0.75	0.00	0.71	0.75	0.66	0.54	0.41	0.70
glszm_SmallAreaLowGrayLevelEmphasis	0.00	0.74	0.00	0.71	0.79	0.62	0.54	0.44	0.67
glrlm_ShortRunLowGrayLevelEmphasis	0.00	0.74	0.00	0.70	0.73	0.66	0.50	0.36	0.68
glrlm_LowGrayLevelRunEmphasis	0.00	0.74	0.00	0.70	0.73	0.67	0.51	0.37	0.68
glszm_LowGrayLevelZoneEmphasis	0.00	0.74	0.00	0.71	0.80	0.60	0.53	0.44	0.65
gldm_LowGrayLevelEmphasis	0.00	0.74	0.00	0.70	0.73	0.67	0.51	0.37	0.68
glrlm_LongRunLowGrayLevelEmphasis	0.00	0.73	0.00	0.70	0.77	0.61	0.52	0.42	0.65
glcm_Idmn	0.00	0.73	0.97	0.69	0.70	0.69	0.50	0.56	0.42
glcm_Idn	0.00	0.73	0.89	0.69	0.67	0.71	0.50	0.55	0.44
glcm_JointEntropy	0.00	0.72	10.37	0.67	0.56	0.81	0.45	0.23	0.74
gldm_DependenceEntropy	0.00	0.72	6.41	0.65	0.51	0.81	0.42	0.15	0.75
glcm_Correlation	0.00	0.72	0.41	0.68	0.75	0.61	0.50	0.62	0.35
shape_MeshVolume	0.00	0.72	5112.34	0.69	0.82	0.52	0.62	0.70	0.53
shape_VoxelVolume	0.00	0.71	7002.50	0.68	0.72	0.62	0.64	0.68	0.58
glrlm_RunLengthNonUniformity	0.00	0.71	5162.89	0.68	0.72	0.63	0.62	0.64	0.58
glszm_LargeAreaLowGrayLevelEmphasis	0.00	0.71	0.00	0.68	0.61	0.75	0.45	0.22	0.75
glszm_SizeZoneNonUniformity	0.00	0.71	3785.52	0.68	0.72	0.63	0.61	0.64	0.56
gldm_DependenceNonUniformity	0.00	0.71	3508.83	0.68	0.72	0.63	0.61	0.64	0.56
shape_SurfaceVolumeRatio	0.00	0.70	0.61	0.68	0.77	0.57	0.61	0.67	0.53
ngtdm_Coarseness	0.00	0.70	0.00	0.67	0.82	0.50	0.63	0.73	0.51
glrlm_GrayLevelNonUniformity	0.00	0.70	138.88	0.68	0.73	0.61	0.64	0.71	0.54
glszm_GrayLevelNonUniformity	0.00	0.70	120.90	0.68	0.73	0.61	0.63	0.70	0.54
glszm_ZoneEntropy	0.00	0.70	6.01	0.67	0.73	0.58	0.45	0.38	0.54
gldm_GrayLevelNonUniformity	0.00	0.70	144.44	0.68	0.73	0.61	0.64	0.71	0.54
shape_SurfaceArea	0.00	0.70	3647.55	0.66	0.74	0.55	0.65	0.67	0.61
glcm_MaximumProbability	0.00	0.70	0.00	0.66	0.48	0.88	0.45	0.19	0.79
glcm_JointEnergy	0.00	0.69	0.00	0.66	0.54	0.80	0.46	0.21	0.79
gldm_LargeDependenceLowGrayLevelEmphasis	0.00	0.69	0.00	0.67	0.65	0.69	0.44	0.23	0.70
shape_LeastAxisLength	0.00	0.69	13.25	0.67	0.85	0.44	0.61	0.78	0.39
shape_Maximum2DDiameterColumn	0.00	0.68	48.62	0.65	0.63	0.67	0.62	0.55	0.70
glcm_SumEntropy	0.00	0.68	6.07	0.65	0.70	0.60	0.44	0.27	0.65
gldm_LargeDependenceHighGrayLevelEmphasis	0.00	0.67	2486.59	0.65	0.51	0.83	0.45	0.21	0.75

shape_MinorAxisLength	0.00	0.67	28.72	0.62	0.54	0.72	0.62	0.51	0.77
firstorder_Maximum	0.00	0.67	126.50	0.68	0.78	0.56	0.51	0.45	0.58
glszm_LargeAreaHighGrayLevelEmphasis	0.00	0.67	2059.42	0.65	0.49	0.83	0.44	0.18	0.77
ngtdm_Busyness	0.00	0.66	0.19	0.67	0.87	0.41	0.60	0.85	0.28
shape_Maximum2DDiameterSlice	0.00	0.66	41.32	0.64	0.66	0.61	0.57	0.55	0.60
glrlm_RunEntropy	0.00	0.66	5.60	0.65	0.70	0.57	0.43	0.27	0.63
firstorder_Range	0.00	0.65	192.50	0.63	0.66	0.60	0.48	0.29	0.72
glcm_Autocorrelation	0.00	0.65	1236.73	0.64	0.53	0.78	0.45	0.21	0.75
shape_Maximum3DDiameter	0.00	0.65	57.12	0.65	0.68	0.61	0.60	0.59	0.61
glcm_JointAverage	0.00	0.65	34.64	0.65	0.51	0.81	0.45	0.21	0.77
glcm_SumAverage	0.00	0.65	69.27	0.65	0.51	0.81	0.45	0.21	0.77
shape_Maximum2DDiameterRow	0.00	0.65	33.48	0.62	0.72	0.51	0.63	0.68	0.56
glcm_ClusterProminence	0.00	0.65	281367.25	0.66	0.72	0.57	0.43	0.29	0.61
ngtdm_Strength	0.00	0.65	2.22	0.65	0.76	0.51	0.62	0.75	0.44
glcm_ClusterTendency	0.00	0.65	303.10	0.65	0.71	0.57	0.43	0.29	0.61
glrlm_LongRunHighGrayLevelEmphasis	0.00	0.64	1422.50	0.64	0.56	0.73	0.45	0.23	0.74
firstorder_Skewness	0.00	0.64	0.23	0.63	0.63	0.63	0.60	0.58	0.63
glszm_HighGrayLevelZoneEmphasis	0.00	0.64	1398.57	0.63	0.50	0.79	0.43	0.15	0.79
glszm_SizeZoneNonUniformityNormalized	0.00	0.64	0.80	0.65	0.73	0.54	0.57	0.79	0.28
glrlm_HighGrayLevelRunEmphasis	0.01	0.64	1380.57	0.63	0.51	0.78	0.44	0.16	0.79
glszm_SmallAreaEmphasis	0.00	0.64	0.91	0.65	0.77	0.50	0.58	0.81	0.28
ngtdm_Complexity	0.01	0.64	9374.40	0.62	0.70	0.52	0.48	0.34	0.65
gldm_HighGrayLevelEmphasis	0.01	0.64	1374.76	0.63	0.51	0.78	0.45	0.18	0.79
gldm_SmallDependenceEmphasis	0.01	0.64	0.83	0.65	0.77	0.49	0.58	0.81	0.28
glrlm_ShortRunHighGrayLevelEmphasis	0.01	0.63	1343.93	0.62	0.51	0.77	0.44	0.16	0.79
glszm_ZonePercentage	0.01	0.63	0.88	0.64	0.72	0.54	0.55	0.77	0.28
gldm_DependenceNonUniformityNormalized	0.01	0.63	0.65	0.65	0.77	0.49	0.58	0.81	0.28
ngtdm_Contrast	0.01	0.63	0.32	0.59	0.42	0.78	0.59	0.67	0.49
glszm_LargeAreaEmphasis	0.01	0.63	1.45	0.64	0.79	0.47	0.58	0.82	0.28
glrlm_RunPercentage	0.01	0.63	0.97	0.64	0.79	0.47	0.58	0.82	0.28
glrlm_RunVariance	0.01	0.63	0.03	0.63	0.77	0.47	0.58	0.81	0.28
glszm_ZoneVariance	0.01	0.63	0.18	0.63	0.70	0.54	0.56	0.75	0.32
glrlm_LongRunEmphasis	0.01	0.63	1.10	0.64	0.78	0.47	0.58	0.81	0.28
glrlm_RunLengthNonUniformityNormalized	0.01	0.63	0.94	0.65	0.79	0.47	0.58	0.82	0.28
glrlm_ShortRunEmphasis	0.01	0.63	0.98	0.64	0.78	0.47	0.58	0.82	0.28
glszm_SmallAreaHighGrayLevelEmphasis	0.01	0.63	1304.59	0.62	0.48	0.79	0.44	0.15	0.81
gldm_LargeDependenceEmphasis	0.01	0.63	1.79	0.64	0.79	0.45	0.59	0.84	0.28
firstorder_Entropy	0.01	0.63	5.48	0.62	0.60	0.66	0.42	0.15	0.77
shape_MajorAxisLength	0.01	0.62	42.09	0.61	0.73	0.47	0.62	0.64	0.58
firstorder_90Percentile	0.01	0.62	82.80	0.62	0.60	0.64	0.46	0.29	0.68
glcm_SumSquares	0.01	0.62	118.42	0.62	0.58	0.66	0.43	0.16	0.77
gldm_DependenceVariance	0.02	0.62	0.24	0.63	0.84	0.39	0.59	0.86	0.25
gldm_SmallDependenceHighGrayLevelEmphasis	0.02	0.62	1190.71	0.61	0.47	0.78	0.44	0.15	0.81
glszm_GrayLevelNonUniformityNormalized	0.02	0.62	0.03	0.62	0.62	0.62	0.41	0.18	0.70
glrlm_GrayLevelNonUniformityNormalized	0.02	0.62	0.03	0.61	0.60	0.62	0.42	0.18	0.74
firstorder_Uniformity	0.02	0.62	0.03	0.61	0.58	0.64	0.44	0.19	0.75
firstorder_RootMeanSquared	0.03	0.61	49.96	0.61	0.60	0.62	0.48	0.36	0.65
firstorder_Variance	0.05	0.61	1018.4	0.62	0.70	0.52	0.39	0.22	0.61

	2								
glrlm_GrayLevelVariance	0.05	0.61	114.52	0.62	0.70	0.52	0.39	0.22	0.61
gldm_GrayLevelVariance	0.05	0.61	113.23	0.62	0.70	0.52	0.39	0.22	0.61
glszm_GrayLevelVariance	0.05	0.61	119.15	0.62	0.70	0.53	0.39	0.22	0.61

Table 3. Cross-validation and external validation performance of models using only radiomic features and using radiomic features + clinical variables to differentiate between low-grade and high-grade pancreatic IPMN patients.

	Radiomics-only		Radiomics + Surgical indication variables	
	CV mean [95% CI]	External Validation	CV mean [95% CI]	External Validation
AUC	0.80 [0.74 - 0.87]	0.81	0.82 [0.76 - 0.88]	0.77
Acc	0.75 [0.73 - 0.77]	0.72	0.77 [0.74 - 0.79]	0.67
Se	0.72 [0.68 - 0.75]	0.68	0.74 [0.69 - 0.78]	0.62
Spe	0.78 [0.75 - 0.81]	0.76	0.79 [0.76 - 0.81]	0.70
PPV	0.70 [0.68 - 0.73]	0.68	0.71 [0.68 - 0.74]	0.61
NPV	0.81 [0.79 - 0.83]	0.76	0.83 [0.80 - 0.86]	0.72
MCC	0.50 [0.46 - 0.54]	0.43	0.53 [0.48 - 0.58]	0.33

(CV) : cross-validation ; (AUC) : Area Under the receiver operating characteristic Curve ; (Acc) : accuracy ; (Se) : sensitivity ; (Spe) : specificity ; (PPV) : positive predictive values ; (NPV) : negative predictive values; (MCC) : Matthews Correlation Coefficient

Table 4. Cross-validation and external validation performance of models using only radiomic features and using radiomic features + clinical variables for the differentiation between patients with low-grade, high-grade, and invasive pancreatic IPMNs.

	Radiomics-only		Radiomics + Surgical indication variables	
	CV mean [95% CI]	External Validation	CV mean [95% CI]	External Validation
AUC	0.81 [na]	0.73	0.81 [na]	0.73
Acc	0.72 [0.70 - 0.75]	0.62	0.75 [0.73 - 0.76]	0.63
Se	0.72 [0.69 - 0.75]	Low-Grade	0.74 [0.73 - 0.76]	Low-Grade
		High-Grade		High-Grade
Se	0.72 [0.69 - 0.75]	Invasive	0.74 [0.73 - 0.76]	Invasive
Se	0.72 [0.69 - 0.75]	0.67	0.74 [0.73 - 0.76]	0.63
Spe	0.86 [0.84 - 0.87]	0.67	0.87 [0.86 - 0.87]	0.71
PPV	0.75 [0.72 - 0.77]	0.60	0.77 [0.75 - 0.78]	0.62
NPV	0.86 [0.85 - 0.87]	0.73	0.87 [0.86 - 0.88]	0.72
MCC	0.58 [0.54 - 0.62]	0.41	0.61 [0.59 - 0.63]	0.43

CV : cross-validation ; AUC : Area Under the receiver operating characteristic Curve ; Acc : accuracy ; Se ; sensitivity ; PPV : positive predictive values ; NPV : negative predictive values; MCC : Matthews Correlation Coefficient

Table 5. Cross-validation and external validation performance of models using only radiomic features and using radiomic features + clinical variables to differentiate between patients with

high-grade and invasive pancreatic IPMNs.

	Radiomics-only		Radiomics + Surgical indication variables	
	CV mean [95% CI]	External Validation	CV mean [95% CI]	External Validation
AUC	0.92 [0.88 - 0.96]	0.91	0.92 [0.87 - 0.96]	0.92
Acc	0.85 [0.83 - 0.88]	0.83	0.87 [0.84 - 0.89]	0.83
Se	0.81 [0.76 - 0.85]	0.69	0.82 [0.78 - 0.86]	0.69
Spe	0.89 [0.86 - 0.91]	0.95	0.90 [0.88 - 0.92]	0.95
PPV	0.85 [0.82 - 0.88]	0.92	0.86 [0.84 - 0.89]	0.92
NPV	0.87 [0.84 - 0.89]	0.79	0.88 [0.85 - 0.90]	0.79
MCC	0.71 [0.66 - 0.75]	0.67	0.73 [0.68 - 0.78]	0.67

CV : cross-validation ; AUC : Area Under the receiver operating characteristic Curve ; Acc : accuracy ; Se : sensitivity ; Spe : Specificity ; PPV : positive predictive values ; NPV : negative predictive values; MCC : Matthews Correlation Coefficient

Table 6. Cross-validation and external validation performance of models using only radiomic features and using radiomic features + clinical variables to differentiate between low-grade and high-grade pancreatic BD-IPMN patients.

	Radiomics-only		Radiomics + Surgical indication variables	
	CV mean [95% CI]	External Validation	CV mean [95% CI]	External Validation
AUC	0.68 [0.55 - 0.81]	0.58	0.68 [0.55 - 0.81]	0.61
Acc	0.68 [0.63 - 0.72]	0.70	0.50 [0.44 - 0.56]	0.45
Se	0.58 [0.46 - 0.70]	0.50	0.82 [0.73 - 0.90]	0.75
Spe	0.71 [0.63 - 0.79]	0.76	0.40 [0.34 - 0.47]	0.36
PPV	0.47 [0.36 - 0.59]	0.40	0.31 [0.27 - 0.35]	0.27
NPV	0.86 [0.82 - 0.90]	0.83	0.87 [0.81 - 0.94]	0.82
MCC	0.31 [0.20 - 0.41]	0.24	0.20 [0.09 - 0.30]	0.10

CV : cross-validation ; AUC : Area Under the receiver operating characteristic Curve ; Acc : accuracy ; Se : sensitivity ; Spe : specificity ; PPV : positive predictive values ; NPV : negative predictive values; MCC : Matthews Correlation Coefficient

Table 7. Cross-validation and external validation performance of models using only radiomic features and using radiomic features + clinical variables to differentiate between patients with low-grade, high-grade, and invasive pancreatic IPMNs.

	Radiomics-only		Radiomics + Surgical indication variables	
	CV mean [95% CI]	External Validation	CV mean [95% CI]	External Validation
AUC	0.63 [0.05 - 0.05]	0.7686	0.75 [0.06 - 0.06]	0.70
Acc	0.51 [0.46 - 0.56]	0.4615	0.51 [0.45 - 0.56]	0.41
Se	0.36 [0.30 - 0.41]	Low-Grade High-Grade Invasive	0.46 [0.38 - 0.54]	Low-GradeHigh-GradeInvasive

		0.52	0.50	0.17		0.36	0.75	0.17
Spe	0.74 [0.71 - 0.78]	0.36	0.74	0.88	0.76 [0.72 - 0.80]	0.71	0.42	0.97
PPV	0.33 [0.30 - 0.36]	0.59	0.33	0.20	0.48 [0.37 - 0.58]	0.6	0.25	0.50
NPV	0.70 [0.67 - 0.72]	0.29	0.85	0.85	0.75 [0.71 - 0.79]	0.38	0.87	0.86
MCC	0.17 [0.08 - 0.26]		0.03		0.61 [0.59 - 0.63]		0.43	

CV : cross-validation ; AUC : Area Under the receiver operating characteristic Curve ; Acc : accuracy ; Se : sensitivity ; Spe : specificity ; PPV : positive predictive values ; NPV : negative predictive values; MCC : Matthews Correlation Coefficient

Table 8. Cross-validation and external validation performance of models using only radiomic features and using radiomic features + clinical variables to differentiate between patients with high-grade and invasive pancreatic BD-IPMNs.

	Radiomics-only		Radiomics + Surgical indication variables	
	CV mean [95% CI]	External Validation	CV mean [95% CI]	External Validation
AUC	0.66 [0.41 - 0.91]	0.85	0.73 [0.50 - 0.95]	0.88
Acc	0.73 [0.56 - 0.90]	0.71	0.80 [0.69 - 0.91]	0.64
Se	0.29 [0.00 - 0.60]	0.33	0.29 [0.00 - 0.60]	0.17
Spe	0.87 [0.73 - 1.00]	1.00	0.97 [0.90 - 1.00]	1.00
PPV	0.50 [0.13 - 0.87]	1.00	1.00 [1.00 - 1.00]	1.00
NPV	0.71 [0.58 - 0.85]	0.67	0.76 [0.66 - 0.87]	0.62
MCC	0.10 [0.00 - 0.43]	0.47	0.20 [0.00 - 0.47]	0.32

CV : cross-validation ; AUC : Area Under the receiver operating characteristic Curve ; Acc : accuracy ; Se : sensitivity ; Spe : specificity ; PPV : positive predictive values ; NPV : negative predictive values; MCC : Matthews Correlation Coefficient

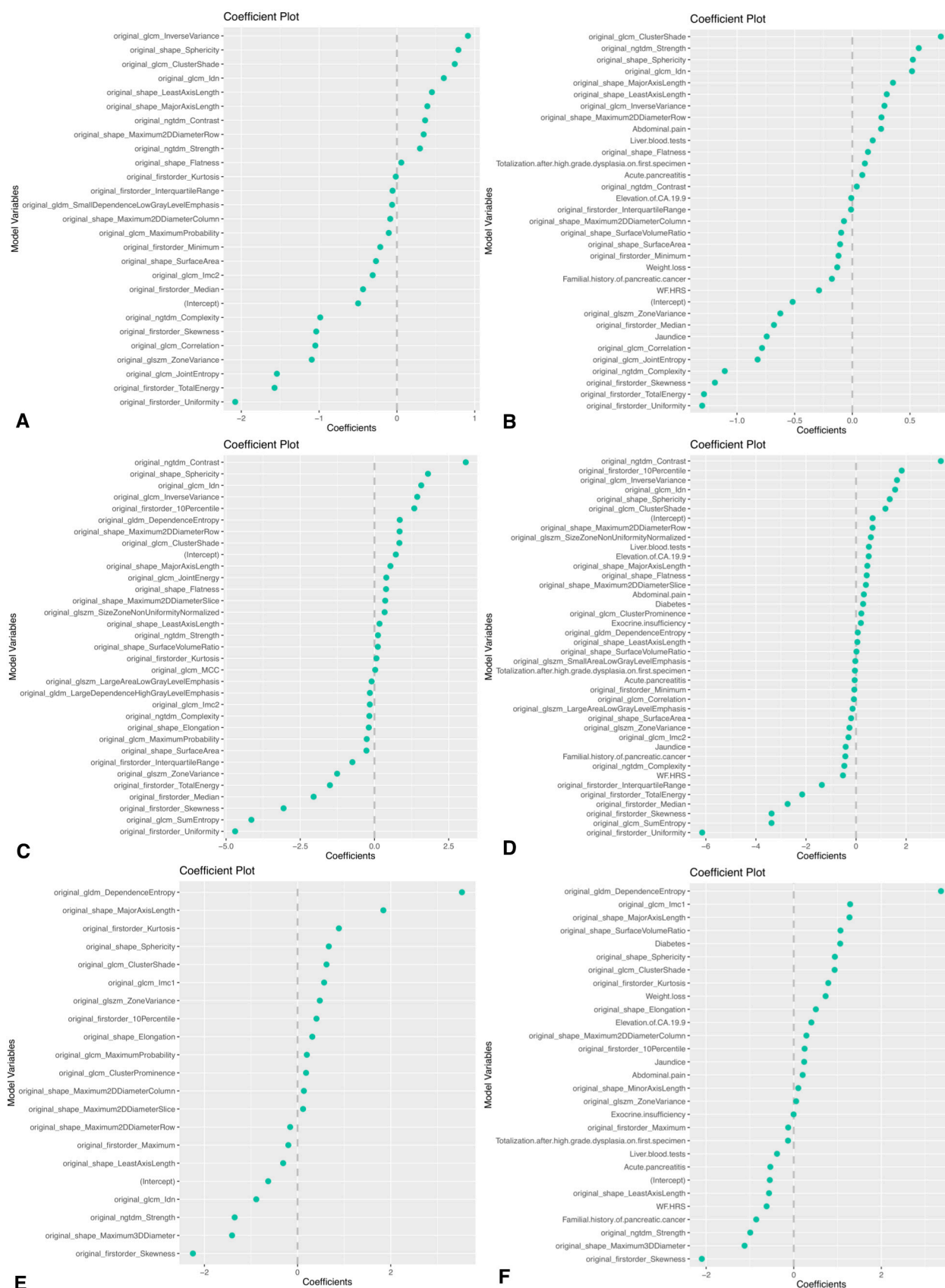


Figure 1. Coefficients of selected variables for (A) radiomics and (B) radiomics + surgical indications models for the differentiation between benign and malignant IPMNs. (C) and (D) provide the coefficients of selected variables for radiomics and radiomics + surgical indications models for the differentiation of low-grade and high-grade dysplasia IPMNs, while (E) and (F) show the

coefficients of radiomics and radiomics + surgical indications models for differentiation between high-grade and invasive IPMNs.



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