

SUPPLEMENTARY MATERIALS

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Supplementary Table 1: List of all studied dosimetric features

Total Dose RT
Vol _{GTV}
Vol _{CTV}
Vol _{PTV}
DMean _{Heart}
V30 _{Heart}
V40 _{Heart}
DMean _{2Lungs}
V13 _{2Lungs}
V20 _{2Lungs}
V30 _{2Lungs}
DMax _{LungH}
DMean _{LungH}
V5 _{LungH}
V10 _{LungH}
V13 _{LungH}
V20 _{LungH}
V30 _{LungH}
DMax _{LungC}
DMean _{LungC}
V5 _{LungC}
V10 _{LungC}
V13 _{LungC}
V20 _{LungC}
V30 _{LungC}

Abbreviations: Vol: volume (mL), GTV: Gross Tumour Volume, CTV: Clinical Tumour Volume, PTV: Planning Tumour Volume, RT: Radiotherapy, DMean_y: Mean Dose received by the y volume, DMax_y: Maximum Dose received by the y volume, V_{xy}: Volume of the y volume receiving x Gy, LungH: Homolateral Lung, LungC: Controlateral Lung, 2Lungs: both lungs

Supplementary Table 2: Main patients' characteristics in the training and testing sets

	Training cohort n = 165		Testing cohort n = 42		<i>p</i>
Age mean (SD)	65.0 (9.38)		65.7 (10.03)		0.67
Gender					
Male (nb, %)	111	67.3	31	73.8	0.42
Female (nb, %)	54	32.7	11	26.2	
Median PS (range)	1	0-2	1	0-2	0.06
Smoking					
Activ (nb, %)	62	37.6	17	40.5	0.52
Former/never (nb, %)	103	62.4	25	59.5	
Known COPD (nb, %)	63 (38.2)		12 (28.6)		0.25
Mean MEVS (% , CI 95%)	74.4 (71.1-77.6)		72.3 (65.7-78.9)		0.58
Histology					
SCC (nb, %)	61	37.0	16	38.1	0.79
ADC (nb, %)	67	40.6	17	40.5	
SCLC (nb, %)	24	14.5	6	14.3	
Others (nb, %)	13	7.9	3	7.1	
AJCC stage (Median)	IIIA		IIIA		0.70
Total RT Dose					
Median (Gy, range)	66.0 (54.0-66.0)		66.0 (54.0-66.0)		0.59
Chemotherapy sequence					
Concomitant (nb, %)	53	32.1	14	33.3	0.99
Induction (nb, %)	48	29.1	12	28.6	
Induction + concomitant (nb, %)	34	20.6	7	16.7	
None (nb, %)	30	18.2	9	21.4	
Adjuvant durvalumab (nb, %)	16	9.7	3	9.5	0.78
APT rate (%)	22.4		19.1		0.64

Abbreviations: SD: Standard Deviation, nb: number, %: percentage, COPD: chronic obstructive pulmonary disease, MEVS: mean expiratory volume/second, SCC: squamous-cell carcinoma, ADC: adenocarcinoma, SCLC: small-cell lung cancer, AJCC: American Joint Commission on Cancer, RT: radiotherapy, APT: Acute pulmonary toxicity \geq grade 2

Supplementary Table 3: Correlation of each feature with the APT risk (training cohort)

Feature	AUC	<i>p</i>
Age	0.52	0.70
Gender	0.52	0.66
COPD	0.57	0.15
MEVS	0.59	0.09
Smoking status	0.57	0.13
AJCC Stage	0.53	0.63
Concomittant CT	0.53	0.56
Neoadjuvant CT	0.52	0.71
Neoadjuvant -> Concomittant CT	0.53	0.38
RT alone	0.50	1.00
Performance Status	0.55	0.27
Total Dose RT	0.51	0.82
VolGTV	0.62	0.03
VolCTV	0.61	0.02
VolPTV	0.62	0.01
DMeanHeart	0.52	0.63
V30Heart	0.51	0.79
V40Heart	0.54	0.43
DMean2Lungs	0.60	0.04
V132Lungs	0.56	0.25
V202Lungs	0.56	0.21
V302Lungs	0.59	0.07
DMaxLungH	0.51	0.86
DMeanLungH	0.60	0.04
V5LungH	0.57	0.17
V10LungH	0.58	0.13
V13LungH	0.58	0.13
V20LungH	0.58	0.12
V30LungH	0.59	0.06
DMaxLungC	0.53	0.61
DMeanLungC	0.51	0.84
V5LungC	0.52	0.78
V10LungC	0.53	0.65
V13LungC	0.50	0.98
V20LungC	0.53	0.61
V30LungC	0.54	0.49
DMeanPmap	0.69	0.0005
LungH_Variance	0.61	0.04
LungH_DVAR	0.53	0.55
LungH_Contrast	0.53	0.57
LungH_IC1	0.50	0.96
LungH_Entropy	0.52	0.65
Lungs_Energy	0.52	0.79

Abbreviations: COPD: Chronic Obstructive Pulmonary Disease, MEVS: mean expiratory volume/second, AJCC: American Joint Committee on Cancer, CT: Chemotherapy, GTV: Gross Tumour Volume, CTV: Clinical Tumour Volume, PTV: Planning Tumour Volume, RT: Radiotherapy, V_{xy} : Volume of the y volume receiving x Gy, $DMean_y$: Mean Dose received by the y volume, $DMax_y$: Maximum Dose received by the y volume, LungH: homolateral lung, Lungs: both lungs, LungH_Variance: Variance extracted from the LungH volume on the Coocurrence matrix (Cooc), LungH_DVAR: Difference Variance extracted from the LungH volume on the Cooc matrix, LungH_Contrast: Contrast extracted from the LungH volume on the Cooc matrix, LungH_ICI: Information measure of correlation extracted from the LungH volume on the Cooc matrix, LungH_Entropy: Entropy extracted from the LungH volume on the Cooc matrix, LungH, Lungs_Energy: Entropy extracted from the LungH volume on the Histogram.

Supplementary Table 4: Analysis of the each model's discrimination between patients with or without APT \geq grade 3 in the training set

Set	AUC	p	Cut-off	C-index	Se	Sp	BAcc	Number of patients, n (%)					
								Below the cutoff (Low risk of APT \geq grade 3)			Above the cutoff (High risk of APT \geq grade 3)		
								Total	Without APT	With APT	Total	Without APT	With APT
Rad _{NoSmote}	0.90	< 0.0001	> 19%	0.87	100.0	74.4	87.2	116 (70.3%)	116 (100.0%)	0 (0.0%)	49 (29.7%)	40 (81.6%)	9 (18.4%)
Rad _{Smote}	0.82	< 0.0001	> 25%	0.82	88.9	75.0	82.0	118 (71.5%)	117 (99.2%)	1 (0.8%)	47 (28.5%)	39 (83.0%)	8 (17.0%)
Pmap _{NoSmote}	0.92	< 0.0001	> 89%	0.92	100.0	84.6	92.3	132 (80.0%)	132 (100.0%)	0 (0.0%)	33 (20.0%)	24 (72.7%)	9 (27.3%)
Pmap _{Smote}	0.91	< 0.0001	> 86%	0.92	100.0	84.6	92.3	132 (80.0%)	132 (100.0%)	0 (0.0%)	33 (20.0%)	24 (72.7%)	9 (27.3%)
Comb _{NoSmote}	0.92	< 0.0001	> 91%	0.92	100.0	84.6	92.3	132 (80.0%)	132 (100.0%)	0 (0.0%)	33 (20.0%)	24 (72.7%)	9 (27.3%)
Comb _{Smote}	0.81	< 0.0001	> 89%	0.83	77.8	87.8	82.8	139 (84.2%)	137 (98.6%)	2 (1.4%)	26 (15.8%)	19 (73.1%)	7 (26.9%)

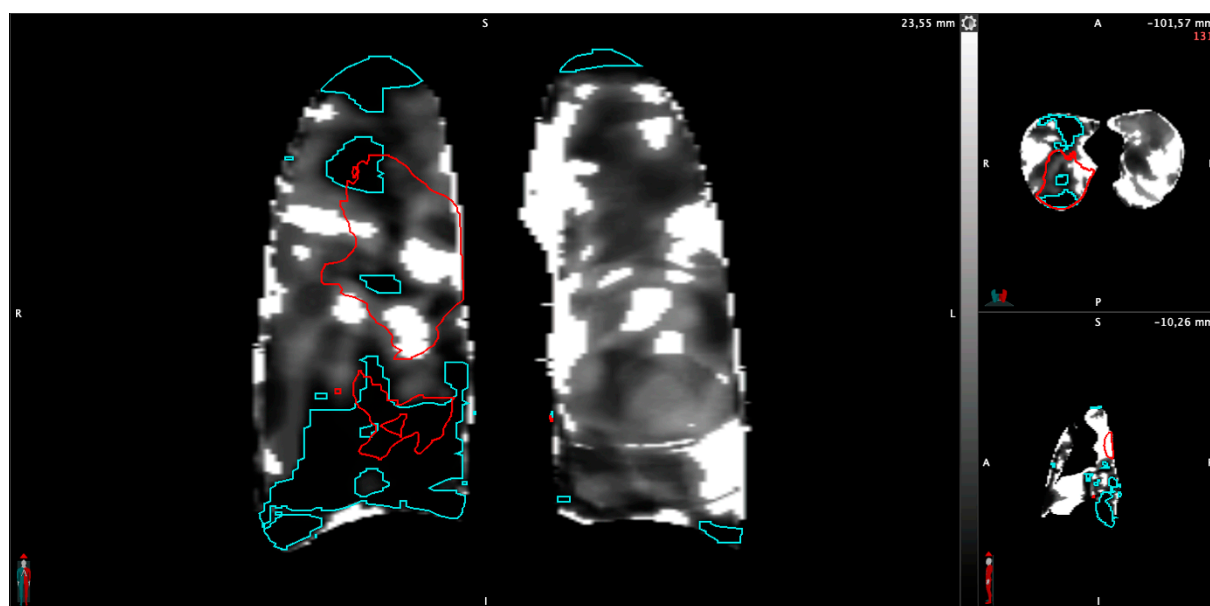
Abbreviations: AUC: Area under the Curve, Se: Sensitivity, Sp: Specificity, BAcc: Balanced Accuracy, APT: Acute Pulmonary Toxicity, Rad_NoSmote: Radiomics-Model without Smote, Rad_Smote: Radiomics-Model with Smote, Pmap_NoSmote: Pmap-Model without Smote, Pmap_Smote: Pmap-Model with Smote, Comb_NoSmote: Combined-Model without Smote, Comb_Smote: Combined-Model with Smote

Supplementary Table 5: Analysis of the each model's discrimination between patients with or without APT \geq grade 3 in the testing set

Set	AUC	p	Cut-off	C-index	Se	Sp	BAcc	Number of patients, n (%)					
								Below the cutoff (Low risk of APT \geq grade 3)			Above the cutoff (High risk of APT \geq grade 3)		
								Total	Without APT	With APT	Total	Without APT	With APT
Rad _{NoSmote}	0.52	0.91	> 19%	0.65	100.0	30.0	65.0	30 (71.4%)	28 (93.3%)	2 (6.7%)	12 (28.6%)	12 (100.0%)	0 (0.0%)
Rad _{Smote}	0.85	0.0001	> 25%	0.89	100.0	77.5	88.8	31 (73.8%)	31 (100.0%)	0 (0.0%)	11 (26.2%)	9 (81.8%)	2 (18.2%)
Pmap _{NoSmote}	0.86	< 0.0001	> 89%	0.90	100.0	80.0	90.0	32 (76.2%)	32 (100.0%)	0 (0.0%)	10 (28.8%)	8 (80.0%)	2 (20.0%)
Pmap _{Smote}	0.89	< 0.0001	> 86%	0.94	100.0	87.5	93.8	35 (83.3%)	35 (100.0%)	0 (0.0%)	7 (16.7%)	5 (71.4%)	2 (28.6%)
Comb _{NoSmote}	0.93	< 0.0001	> 91%	0.91	100.0	82.5	91.3	33 (78.6%)	33 (100.0%)	0 (0.0%)	9 (21.4%)	7 (77.8%)	2 (22.2%)
Comb _{Smote}	0.88	< 0.0001	> 89%	0.86	100.0	72.5	86.3	29 (69.0%)	29 (100.0%)	0 (0.0%)	13 (31.0%)	11 (84.6%)	2 (15.4%)

Abbreviations: AUC: Area under the Curve, Se: Sensitivity, Sp: Specificity, BAcc: Balanced Accuracy, APT: Acute Pulmonary Toxicity, Rad_NoSmote: Radiomics-Model without Smote, Rad_Smote: Radiomics-Model with Smote, Pmap_NoSmote: Pmap-Model without Smote, Pmap_Smote: Pmap-Model with Smote, Comb_NoSmote: Combined-Model without Smote, Comb_Smote: Combined-Model with Smote

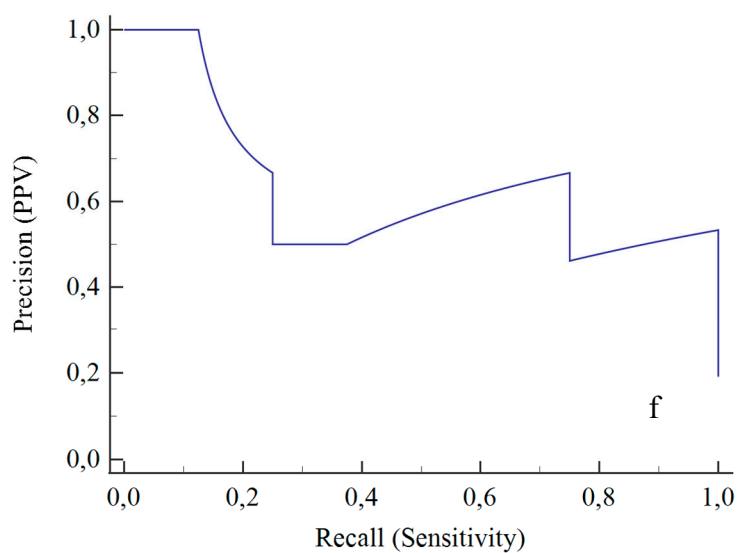
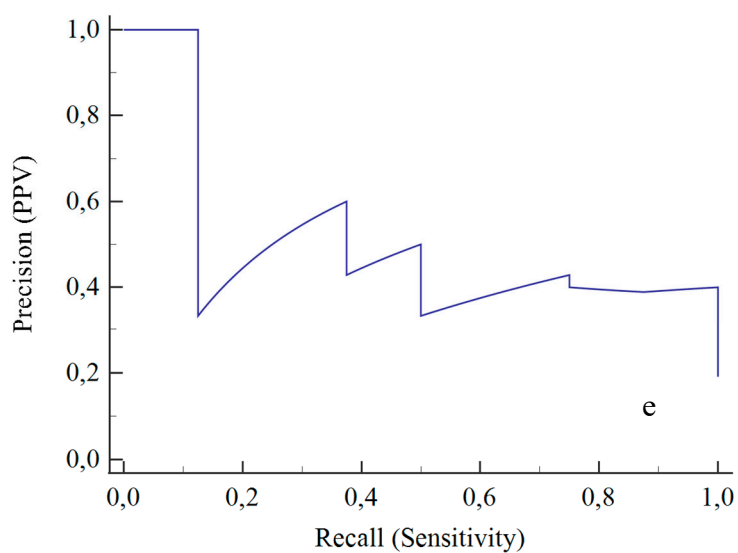
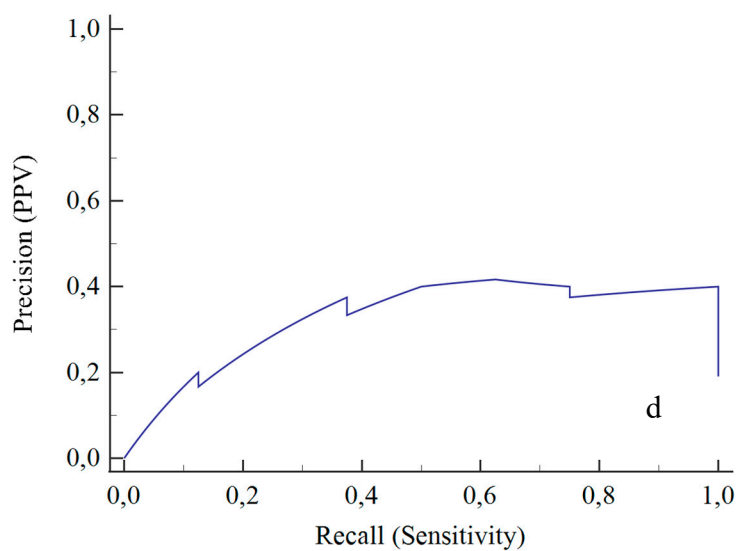
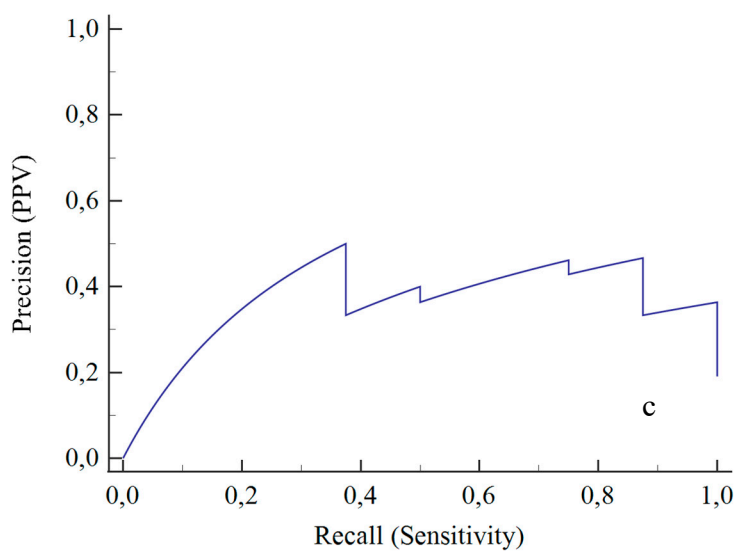
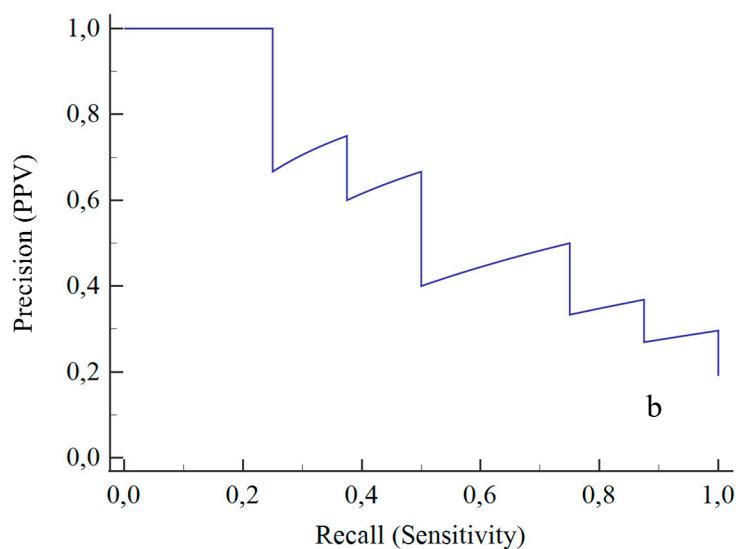
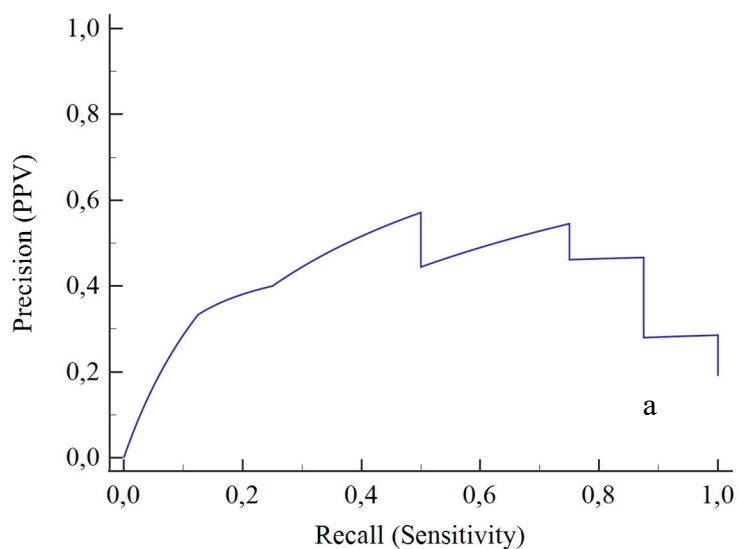
Supplementary Figure 1: Overlap between the PmapRad and the Pmap maps



Caption: Red: Pmap region, blue: PmapRad region

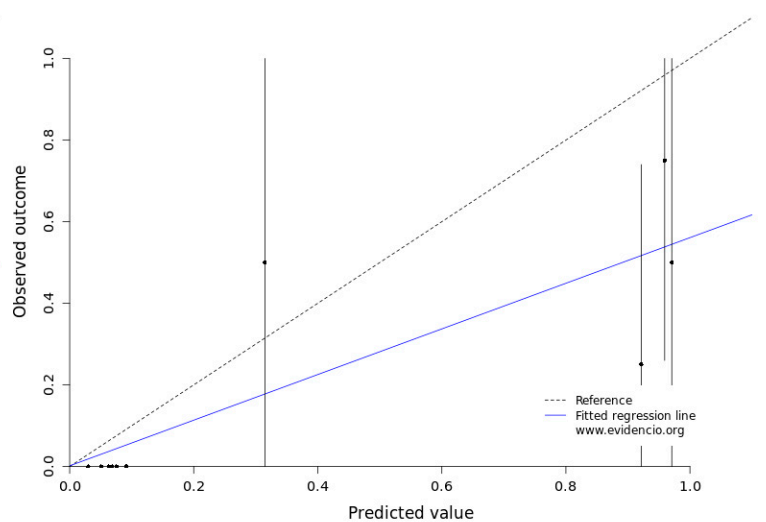
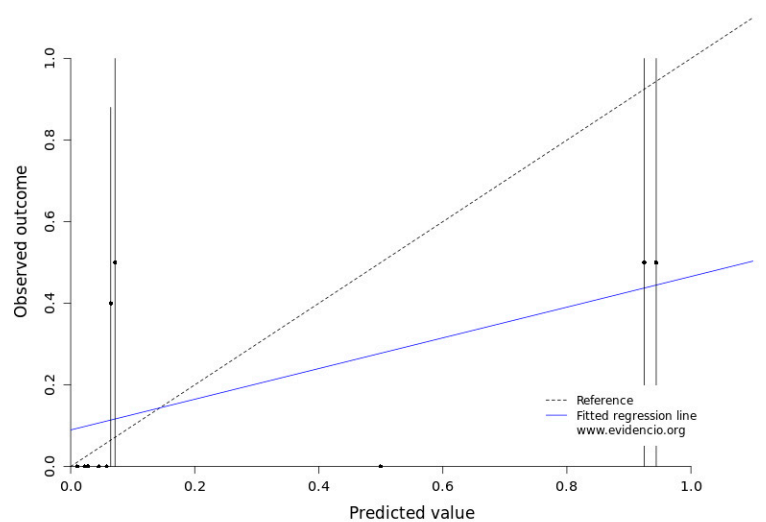
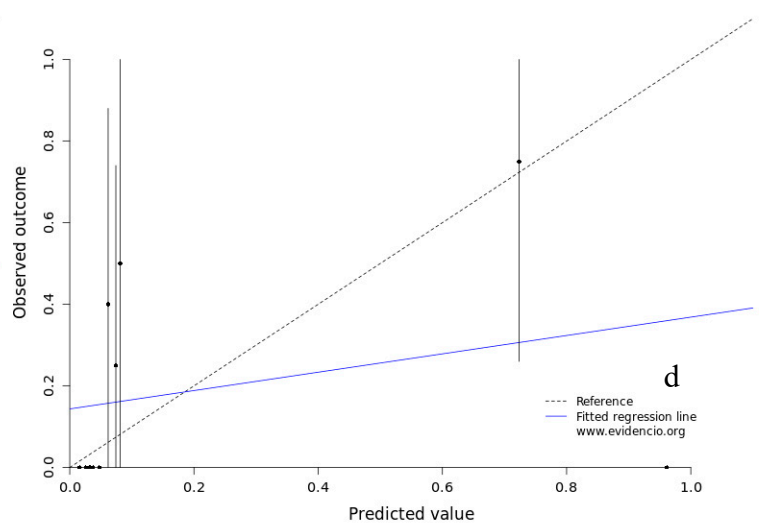
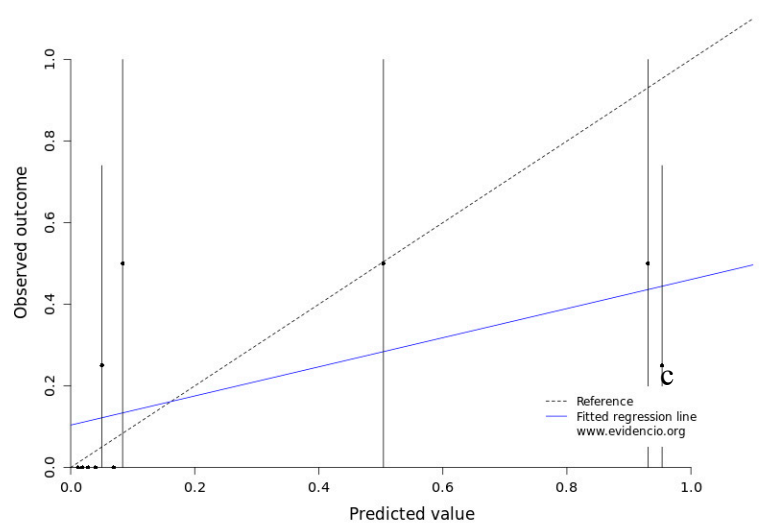
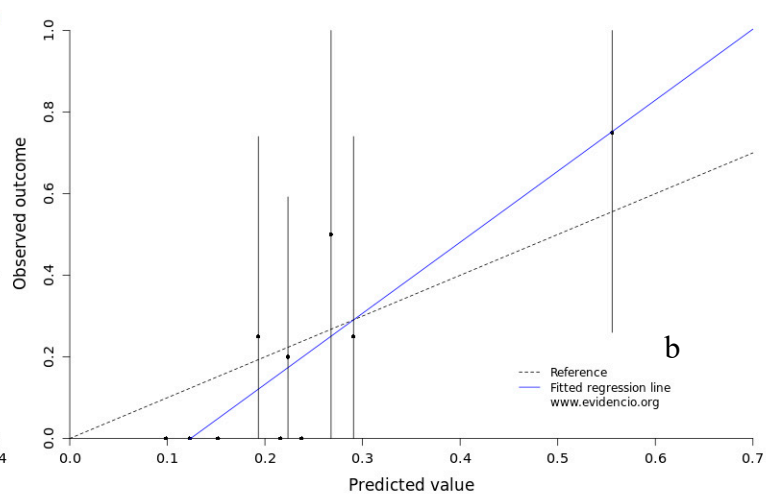
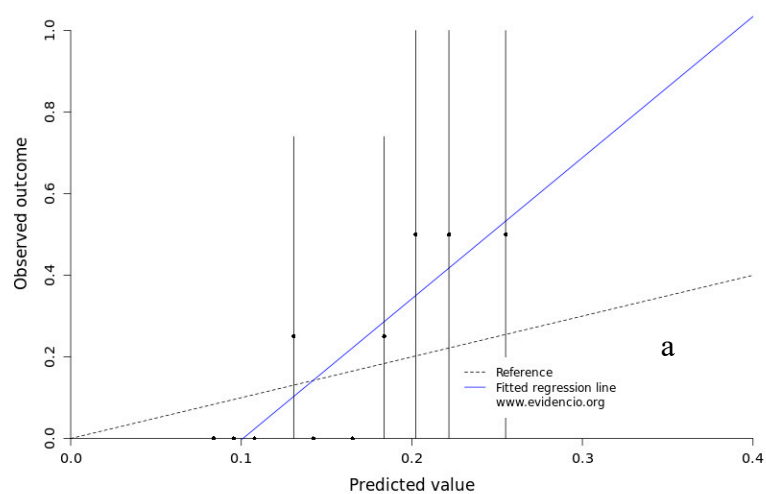
Supplementary Figure 2: Comparison between each model in the testing sets based on the precision-recall curve for the prediction of $\text{APT} \geq \text{grade 2}$

- a: Rad_{NoSmote} model
- b: Rad_{Smote} model
- c: Pmap_{NoSmote} model
- d: Pmap_{Smote} model
- e: Comb_{NoSmote} model
- f: Comb_{Smote} model

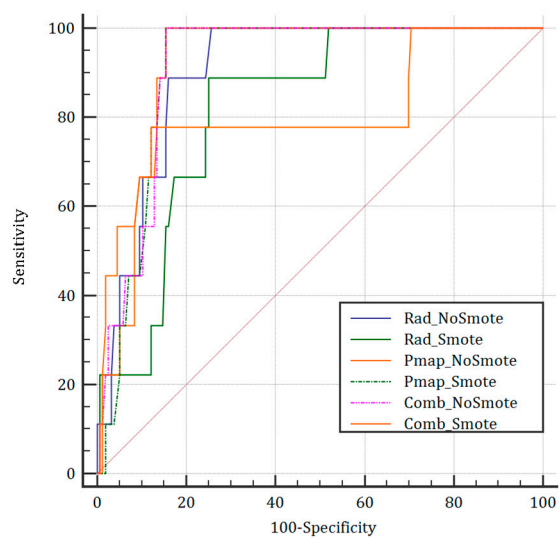


Supplementary Figure 3: Comparison between each model in the testing sets based on the calibration curve for the prediction of APT \geq grade 2

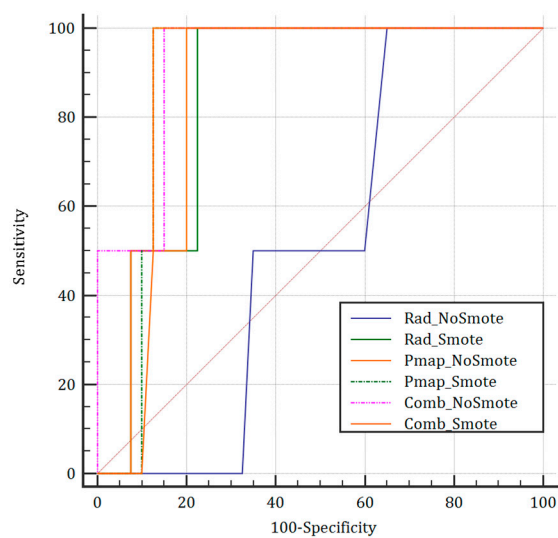
- a: Rad_{NoSmote} model
- b: Rad_{Smote} model
- c: Pmap_{NoSmote} model
- d: Pmap_{Smote} model
- e: Comb_{NoSmote} model
- f: Comb_{Smote} model



Supplementary Figure 4: Comparison between each model in the training (a) and testing (b) sets based on the ROC curve for the prediction of $APT \geq \text{grade } 3$



A

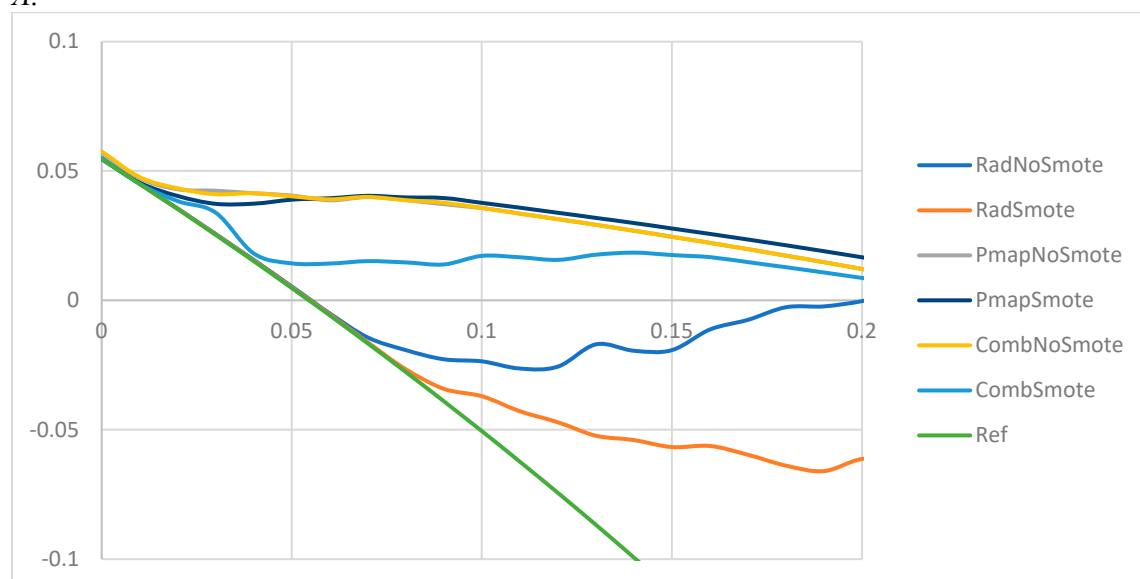


B

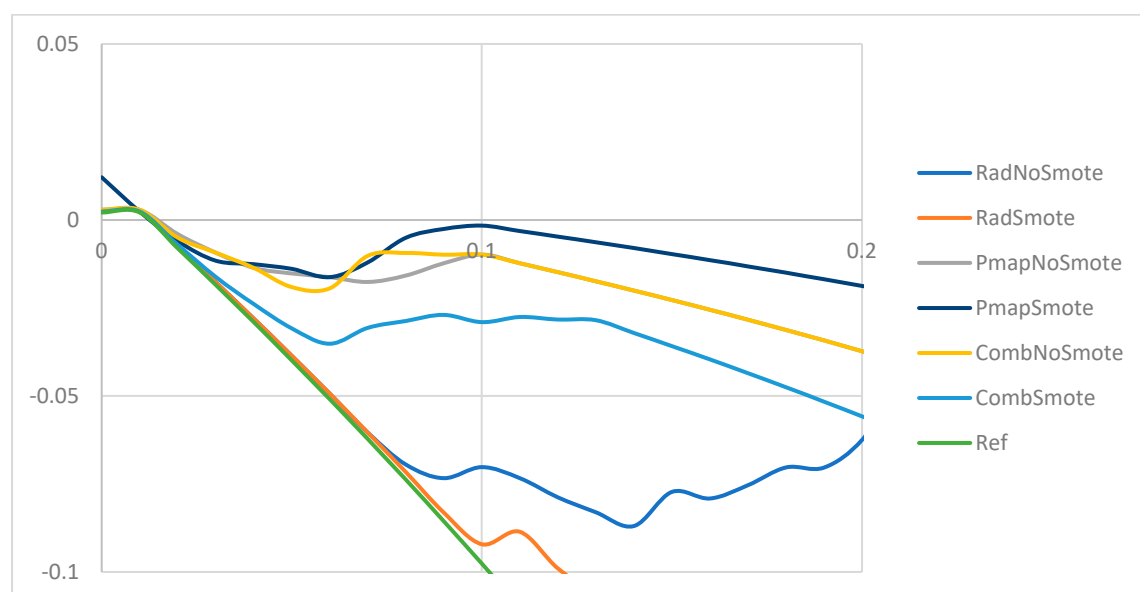
Abbreviation: APT: Acute Pulmonary Toxicity, Rad_NoSmote: Radiomics-Model without Smote, Rad_Smote: Radiomics-Model with Smote, Pmap_NoSmote: Pmap-Model without Smote, Pmap_Smote: Pmap-Model with Smote, Comb_NoSmote: Combined-Model without Smote, Comb_Smote: Combined-Model with Smote

Supplementary Figure 5: Comparison between each model in the training (a) and testing (b) sets based on the Decision Curve Analysis for the prediction of $APT \geq \text{grade } 3$

A.



B.



Abbreviation: APT: Acute Pulmonary Toxicity, Rad_NoSmote: Radiomics-Model without Smote, Rad_Smote: Radiomics-Model with Smote, Pmap_NoSmote: Pmap-Model without Smote, Pmap_Smote: Pmap-Model with Smote, Comb_NoSmote: Combined-Model without Smote, Comb_Smote: Combined-Model with Smote