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Patterns of Locoregional Relapses in Patients with Contemporarily Staged Stage III-N2 NSCLC Treated with Induction Chemotherapy and Resection: Implications for Postoperative Radiotherapy Target Volumes Supplementary material

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Table 1: patient, tumor and treatment characteristics

		INTENTION-TO-TREAT ANALYSIS			PER-PROT	OCOL ANALY	'SIS
Characteristic	All resected patients (N=150)	PORT (N=86)	No-PORT (N=64)	p- value	PORT (N=70)	No-PORT (N=80)	p-value
Age of diagnosis (years)							
Median	61	61	63	0.75	60	64	0.69
Range	34-80	34-80	38-79	-	34-80	38-79	-
Gender							
Male	109 (72.7%)	67 (77.9%)	42 (65.6%)	0.38	54 (77.1%)	55 (68.8%)	1
Female	41 (27.3%)	19 (22.1%)	22 (34.4%)	0.15	16 (22.9%)	25 (31.2%)	0.28
Performance status (WHO)							
0	98 (65.3%)	56 (65.1%)	42 (65.6%)	0.97	46 (64.7%)	52 (65.0%)	0.61
1	49 (32.7%)	29 (33.7%)	20 (31.3%)	0.79	23 (32.9%)	26 (32.5%)	0.67
2	3 (2.0%)	1 (1.2%)	2 (3.1%)	0.40	1 (1.4%)	2 (2.5%)	0.56
Smoking status <sup>a</sup>							
Never smoked	6 (4.0%)	4 (4.7%)	2 (3.1%)	0.64	3 (4.3%)	3 (3.8%)	1
Ex-smoker	62 (41.3%)	39 (45.3%)	23 (35.9%)	0.38	32 (45.7%)	30 (37.5%)	0.80
Active smoker	79 (52.7%)	42 (48.8%)	37 (57.8%)	0.45	34 (48.6%)	45 (56.2%)	0.22
Unknown	3 (2.0%)	1 (1.2%)	2 (3.1%)	0.40	1 (1.4%)	2 (2.5%)	1
Tumor side							
Left	48 (32.0%)	32 (37.2%)	16 (25.0%)	0.19	26 (37.1%)	22 (27.5%)	0.56
Right	102 (68.0%)	54 (62.8%)	48 (75.0%)	0.37	44 (62.9%)	58 (72.5%)	0.20
Tumor location							
Upper-middle	100 66.6%)	56 (65.1%)	44 (68.7%)	0.79	48 (68.6%)	52 (65.0%)	0.77
Lower	50 (33.3%)	30 (34.9%)	20 (31.3%)	0.70	22 (31.4%)	28 (35.0%)	0.40
Histological subtype							
Squamous cell carcinoma	71 (47.3%)	43 (50.0%)	28 (43.7%)	0.58	33 (47.1%)	38 (47.5%)	0.64
Adenocarcinoma	67 (44.7%)	39 (45.3%)	28 (43.7%)	0.89	33 (47.1%)	34 (42.5%)	0.90
Large cell carcinoma	10 (6.7%)	3(3.5%)	7 (10.9%)	0.08	3 (4.3%)	7 (8.8%)	0.21
Other	2 (1.3%)	1 (1.2%)	1 (1.6%)	0.83	1 (1.4%)	1 (1.2%)	1
Mediastinal lymph node							

involvement							
Single station N2	121 (80.7%)	66 (76.7%)	55 (85.9%)	0.53	52 (74.3%)	68 (85.0%)	0.14
Multiple station N2	29 (19.3%)	20 (23.3%)	9 (14.1%)	0.21	18 (25.7%)	12 (15.0%)	0.21
Radiological T-stage							
cT1	27 (18.0%)	12 (14.0%)	15 (23.4%)	0.18	7 (10.0%)	20 (25.0%)	0.01
сТ2	49 (32.7%)	22 (25.6%)	27 (42.2%)	0.08	17 (24.3%)	32 (40.0%)	0.03
сТ3	65 (43.3%)	46 (53.4%)	19 (29.7%)	0.03	40 (57.1%)	25 (31.3%)	0.05
cT4	9 (6.0%)	6 (7.0%)	3 (4.7%)	0.60	6 (8.6%)	3 (3.7%)	0.32
Response after induction chemotherapy (RECIST 1.1)							
Stable	49 (32.7%)	34 (39.5%)	15 (23.4%)	0.08	31 (44.3%)	18 (22.5%)	0.05
Partial	88 (58.7%)	49 (57.0)	39 (60.9%)	0.75	37 (55.7%)	51 (63.7%)	0.14
Complete	13 (8.7%)	3 (3.5%)	10 (15.6%)	0.01	2 (2.9%)	11 (13.7%)	<0.01
Surgery type							
Lobectomy/bilobectomy	116 (77.3%)	61 (70.9%)	55 (85.9%)	0.30	51 (72.9%)	65 (81.3%)	0.19
Pneumonectomy	34 (22.7%)	25 (29.1%)	9 (14.1%)	0.06	19 (27.1%)	15 (18.7%)	0.49
Completeness of resection							
R0	115 (76.7%)	52 (60.5%)	64 (100%)	<0.01	41 (58.6%)	74 (92.5%)	<0.01
R1	29 (19.3%)	28 (32.5%)	0 (0.0%)	<0.01	24 (34.3%)	5 (6.3%)	<0.01
R2	6 (4.0%)	6 (7.0%)	0 (0.0%)	0.03	5 (7.1%)	1 (1.2%)	0.06
Downstaging of mediastinal lymph nodes							
Downstaging	69 (46.0%)	7 (8.1%)	64 (100%)	<0.01	7 (10.0%)	63 (78.8%)	<0.01
Persistent ypN2/3	81 (54.0%)	79 (91.9%)	0 (0.0%)	<0.01	63 (90.0%)	17 (21.2%)	<0.01

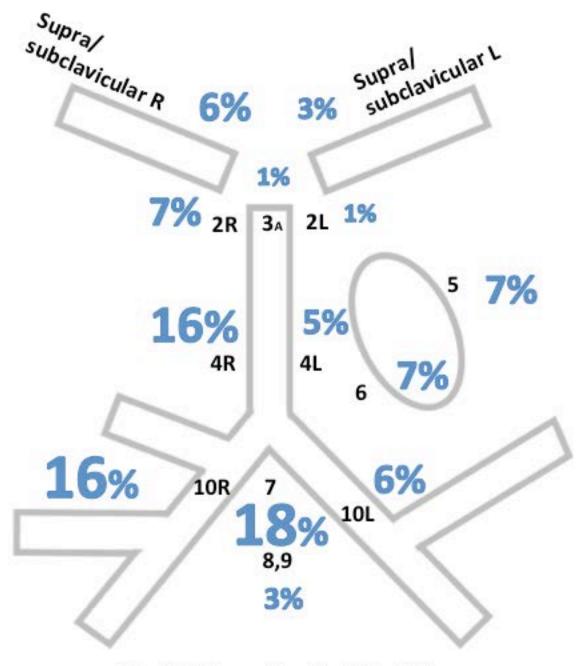
All characteristics are at time of diagnosis. Signifcant p-values (<0.05) are depicted in bold.  $^a$  Ex-smoker: smoking cessation > 1 year

WHO: World Health Organization; PORT: postoperative radiation therapy

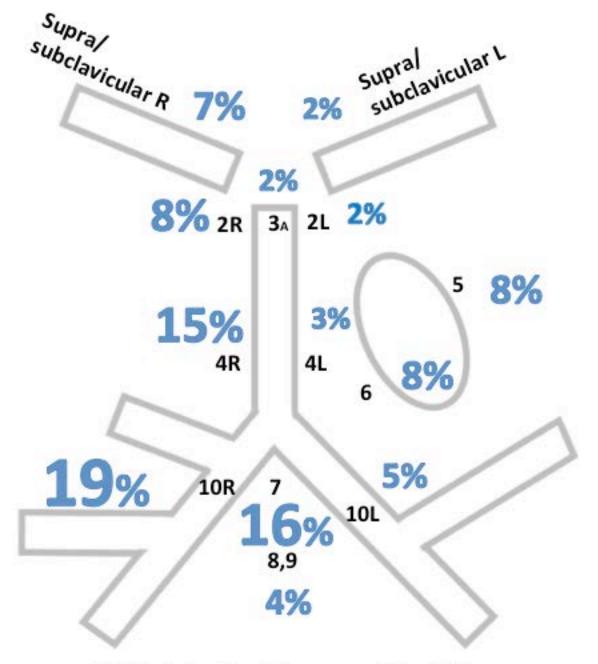
<u>Table 2: Overview of loco-regional relapses per lymph node station in PORT vs non-PORT group</u>

	INTENTION-TO-TREAT			PER-PR		
Number of patients with LR (58/150)	PORT (34/58)	Non-PORT (24/58)	p-value	PORT (26/58)	Non-PORT (32/58)	p-value
Total sites of nodal relapse	99 (100%)	72 (100%)	0.85	58 (100%)	113 (100%)	<0.01
Ipsilateral						
Station 2 Station 4 Hilum (10,11) Sub/Supraclavicular (station 1)	3 (3%) 10 (10%) 15 (15%) 6 (6%)	6 (8%) 13 (18%) 13 (18%) 4 (5%)	0.12 0.14 0.59 0.93	1 (2%) 5 (9%) 12 (21%) 4 (7%)	8 (7%) 18 (16%) 16 (14%) 6 (5%)	<b>0.04 0.02</b> 0.92 0.72
Contralateral						
Station 2 Station 4 Hilum (10,11) Sub/Supraclavicular (station 1)	4 (4%) 9 (9%) 8 (8%) 3 (3%)	1 (1%) 4 (5%) 3 (4%) 3 (4%)	0.33 0.44 0.34 0.67	3 (5%) 3 (5%) 4 (7%) 1 (2%)	2 (2%) 10 (9%) 7 (6%) 5 (4%)	0.52 0.10 0.53 0.15
Station 3A	1 (1%)	1 (1%)	0.80	1 (2%)	1 (1%)	0.90
Station 5	9 (9%)	3 (4%)	0.25	5 (9%)	7 (6%)	0.78
Station 6	9 (9%)	3 (4%)	0.25	5 (9%)	7 (6%)	0.78
Station 7	17 (17%)	13 (18%)	0.83	9 (15%)	21 (19%)	0.08
Station 8,9	2 (2%)	3 (4%)	0.40	2 (3%)	3 (3%)	0.80
Bronchial stump	3 (3%)	2 (3%)	0.95	3 (5%)	2 (2%)	0.52

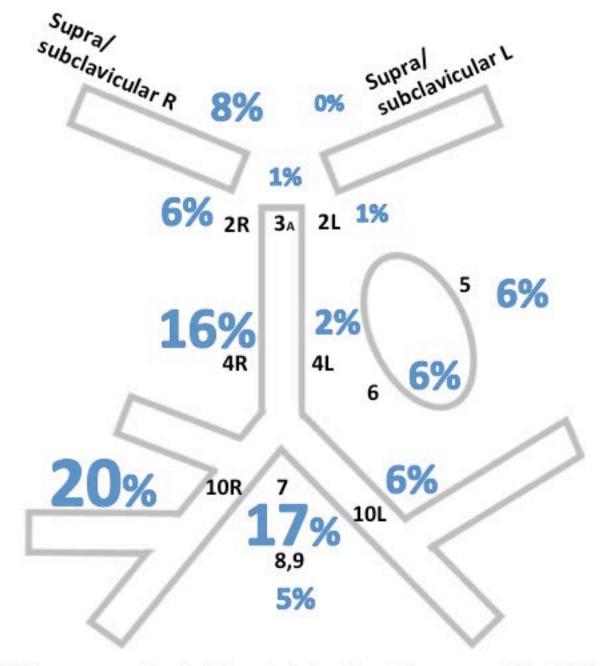
PORT: postoperative radiation therapy



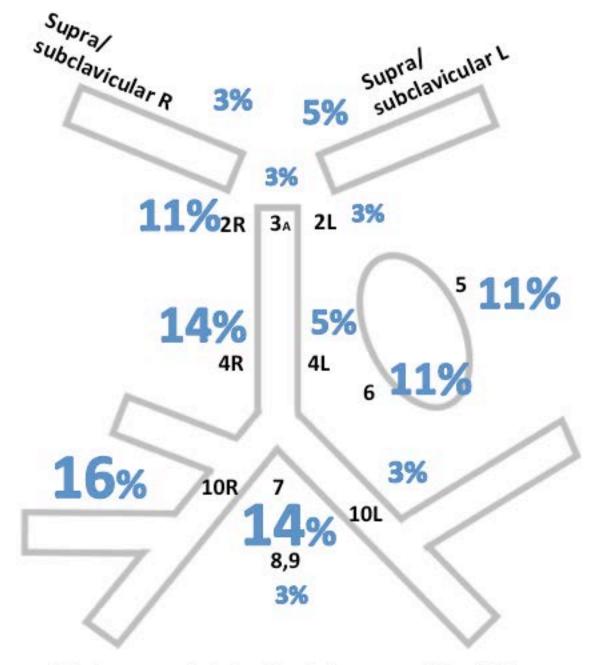
A) All LR patients (N=58)



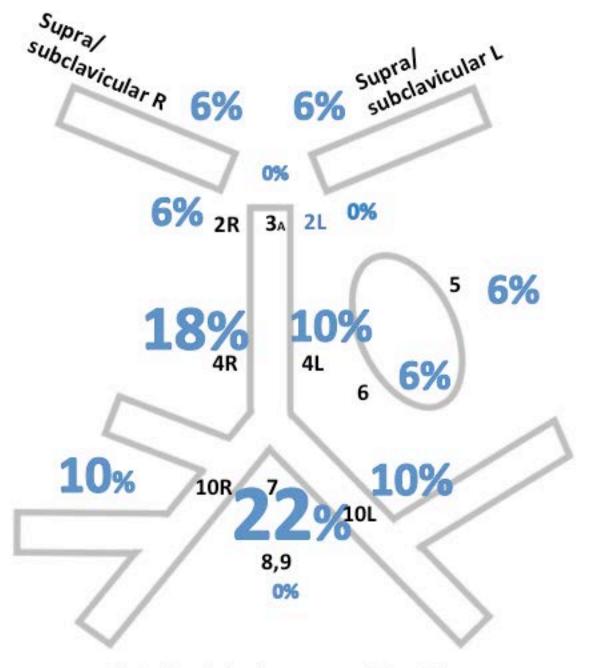
B) Right-sided tumors (N=42)



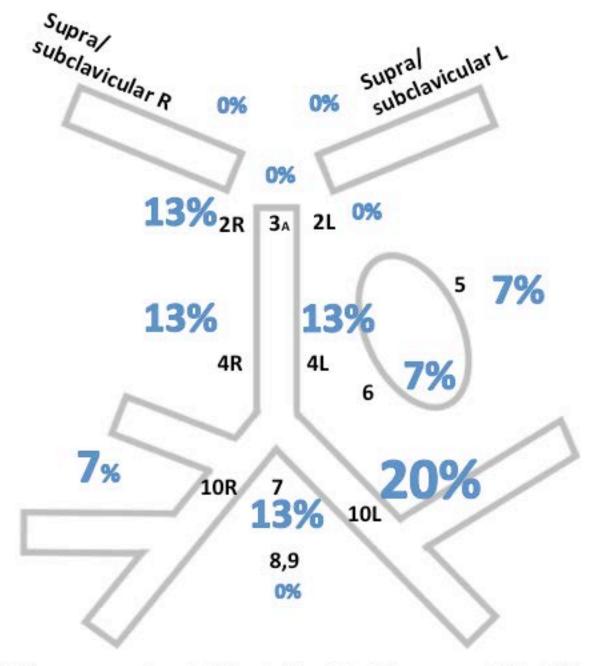
C) Upper and middle right-sided tumors (N=29)



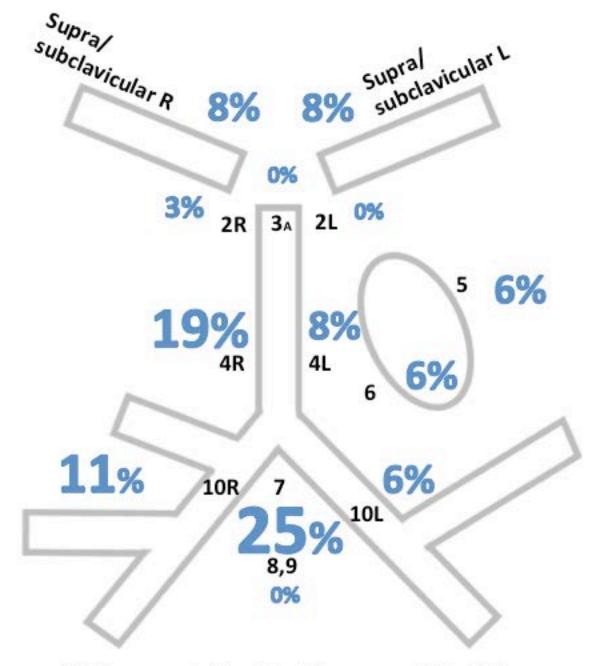
D) Lower right-sided tumors (N=13)



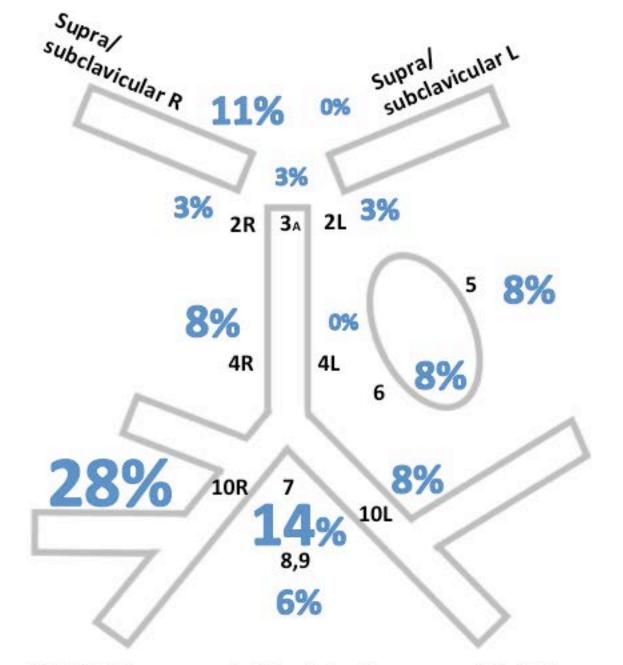
E) Left-sided tumors(N=16)



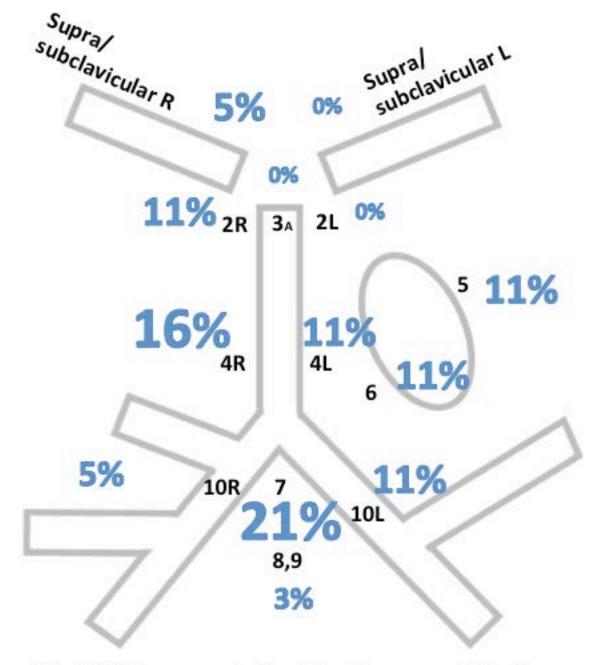
F) Upper and middle left-sided tumors (N=16)



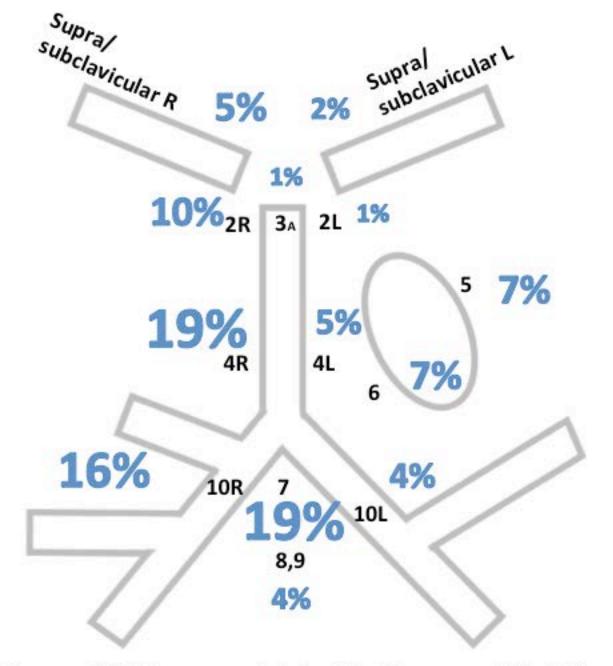
G) Lower left-sided tumors (N=10)



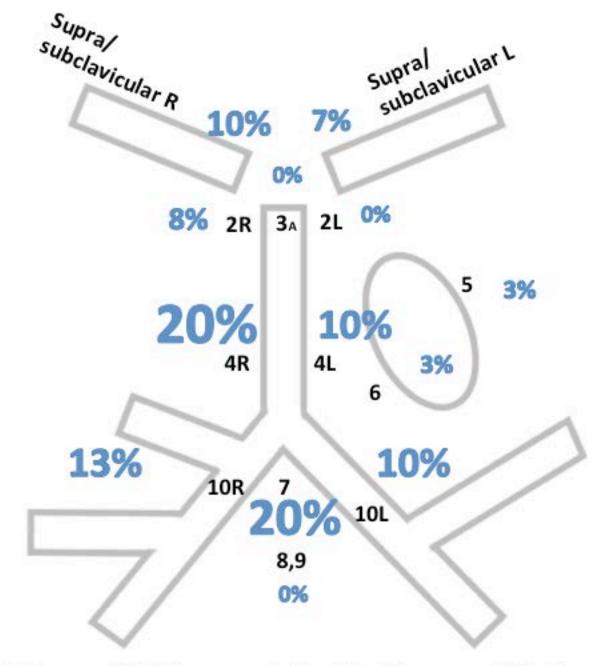
A) PORT group right-sided tumors (N=17)



B) PORT group left-sided tumors (N=9)

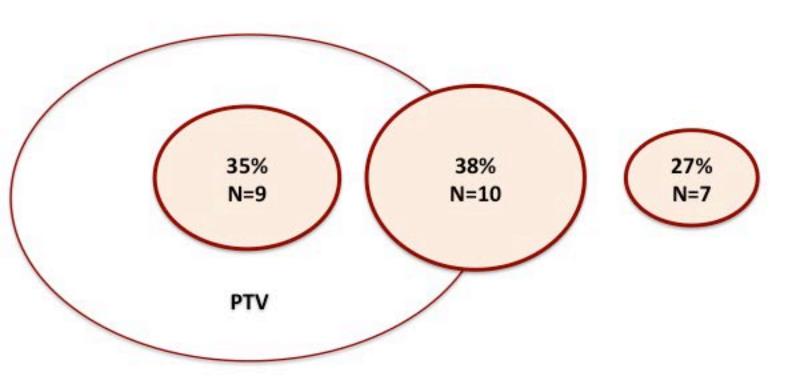


C) non-PORT group right-sided tumors (N=25)



D) non-PORT group left-sided tumors (N=7)

## A. PORT group (N=26)



## B. Non-PORT group (N=32)

