

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-PROTOCOL ANALYSIS | | |
|------------------------------------|----------------------------------|----------------|-------------------|---------|-----------------------|-------------------|---------|
| 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 ^a | | | | | | | |
| 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 |
| cT2 | 49 (32.7%) | 22 (25.6%) | 27 (42.2%) | 0.08 | 17 (24.3%) | 32 (40.0%) | 0.03 |
| cT3 | 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. Significant p-values (<0.05) are depicted in bold.

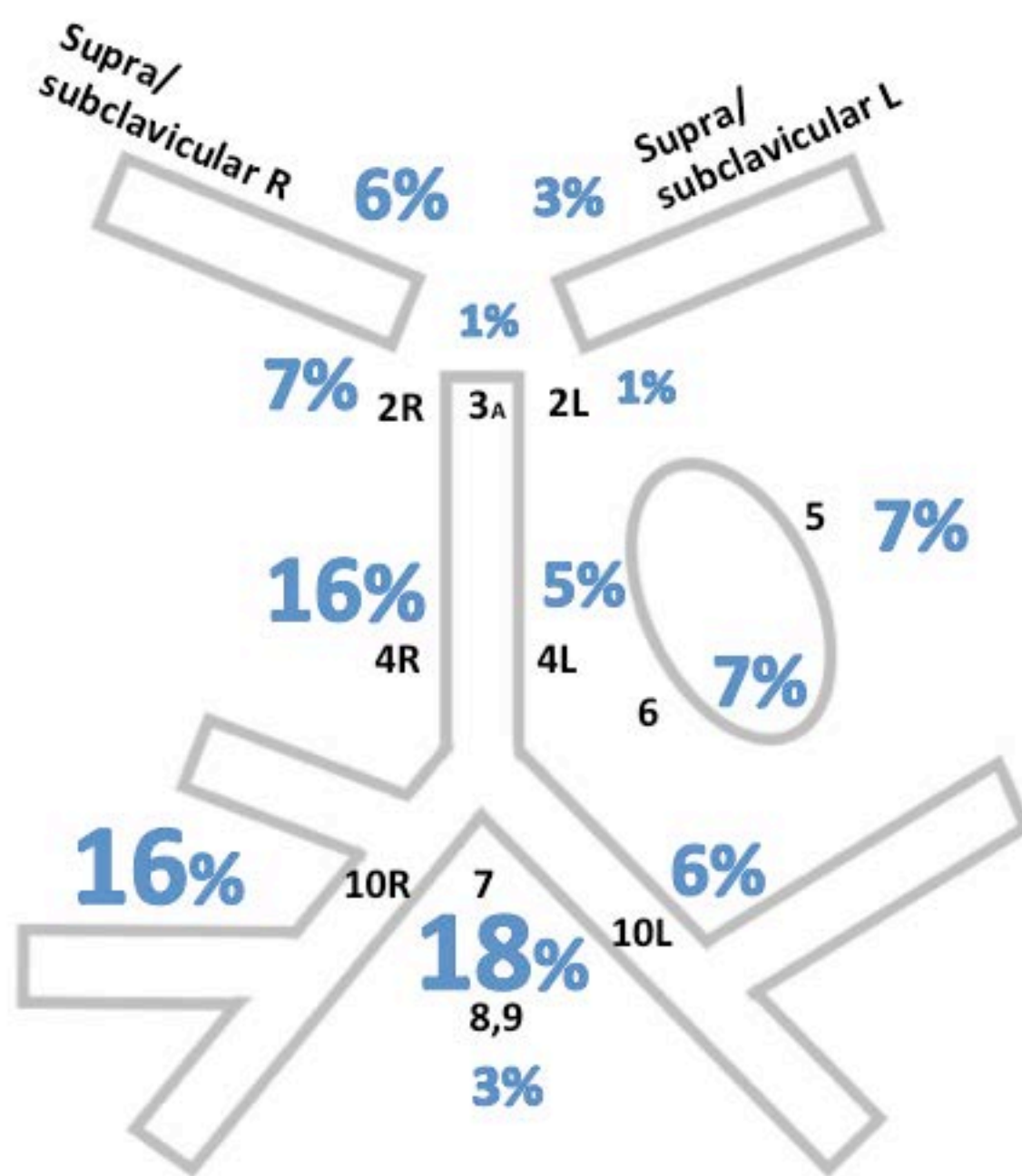
^a Ex-smoker: smoking cessation > 1 year

WHO: World Health Organization; PORT: postoperative radiation therapy

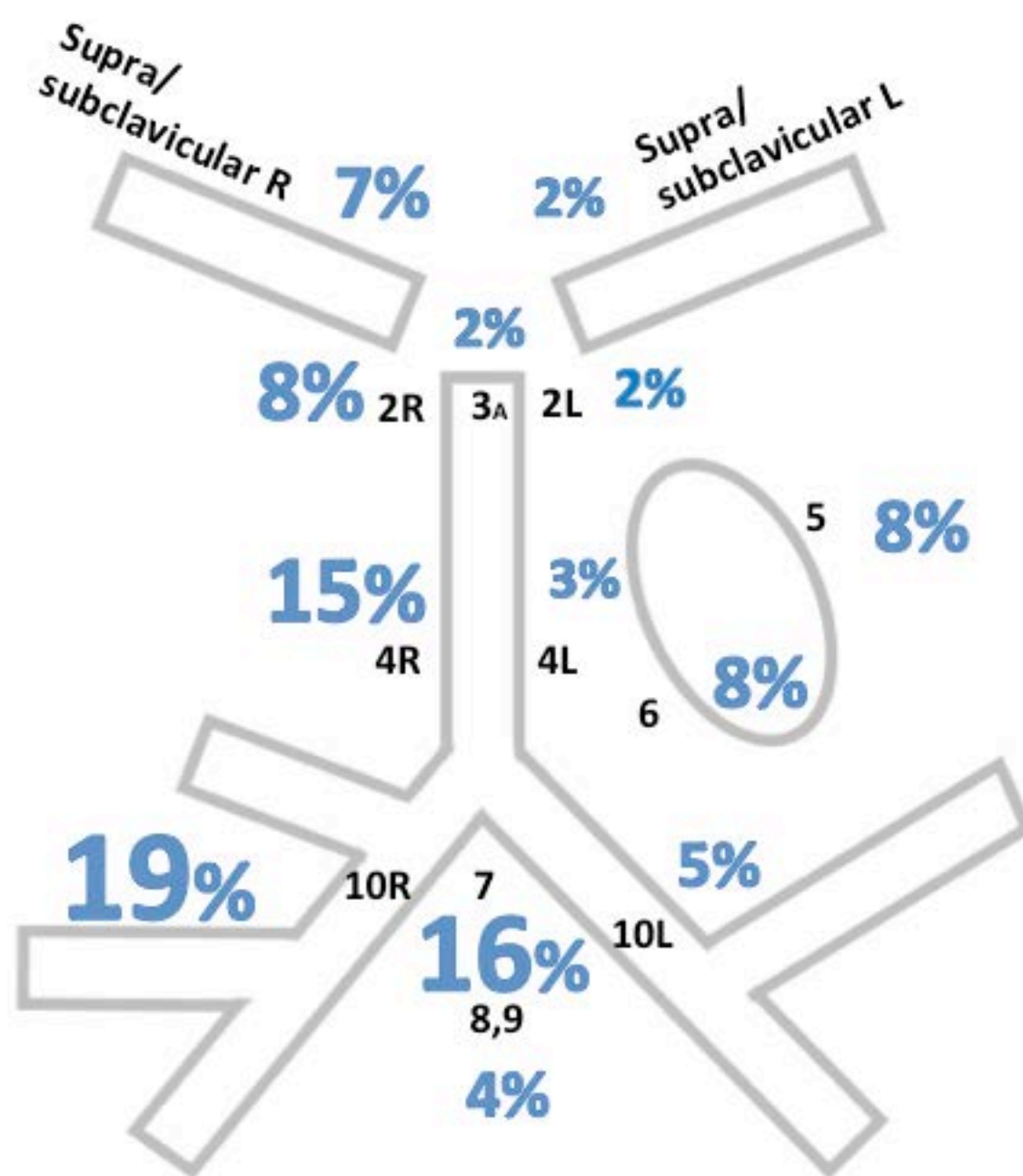
Table 2: Overview of loco-regional relapses per lymph node station in PORT vs non-PORT group

| INTENTION-TO-TREAT | | | | PER-PROTOCOL | | |
|--|--------------|------------------|---------|--------------|------------------|-----------------|
| 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 | 3 (3%) | 6 (8%) | 0.12 | 1 (2%) | 8 (7%) | 0.04 |
| Station 4 | 10 (10%) | 13 (18%) | 0.14 | 5 (9%) | 18 (16%) | 0.02 |
| Hilum (10,11) | 15 (15%) | 13 (18%) | 0.59 | 12 (21%) | 16 (14%) | 0.92 |
| Sub/Supraclavicular (station 1) | 6 (6%) | 4 (5%) | 0.93 | 4 (7%) | 6 (5%) | 0.72 |
| Contralateral | | | | | | |
| Station 2 | 4 (4%) | 1 (1%) | 0.33 | 3 (5%) | 2 (2%) | 0.52 |
| Station 4 | 9 (9%) | 4 (5%) | 0.44 | 3 (5%) | 10 (9%) | 0.10 |
| Hilum (10,11) | 8 (8%) | 3 (4%) | 0.34 | 4 (7%) | 7 (6%) | 0.53 |
| Sub/Supraclavicular (station 1) | 3 (3%) | 3 (4%) | 0.67 | 1 (2%) | 5 (4%) | 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 |

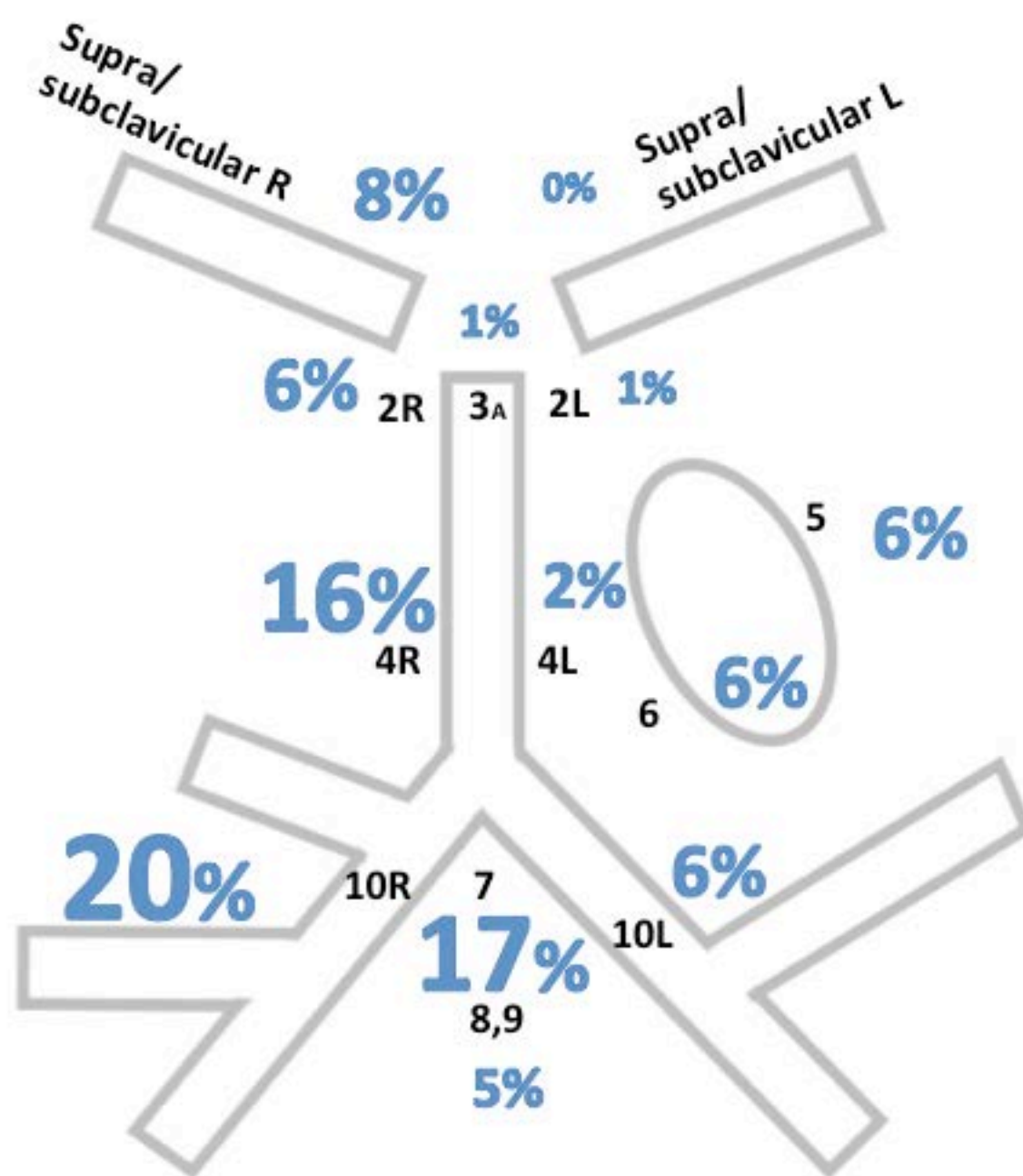
PORT: postoperative radiation therapy



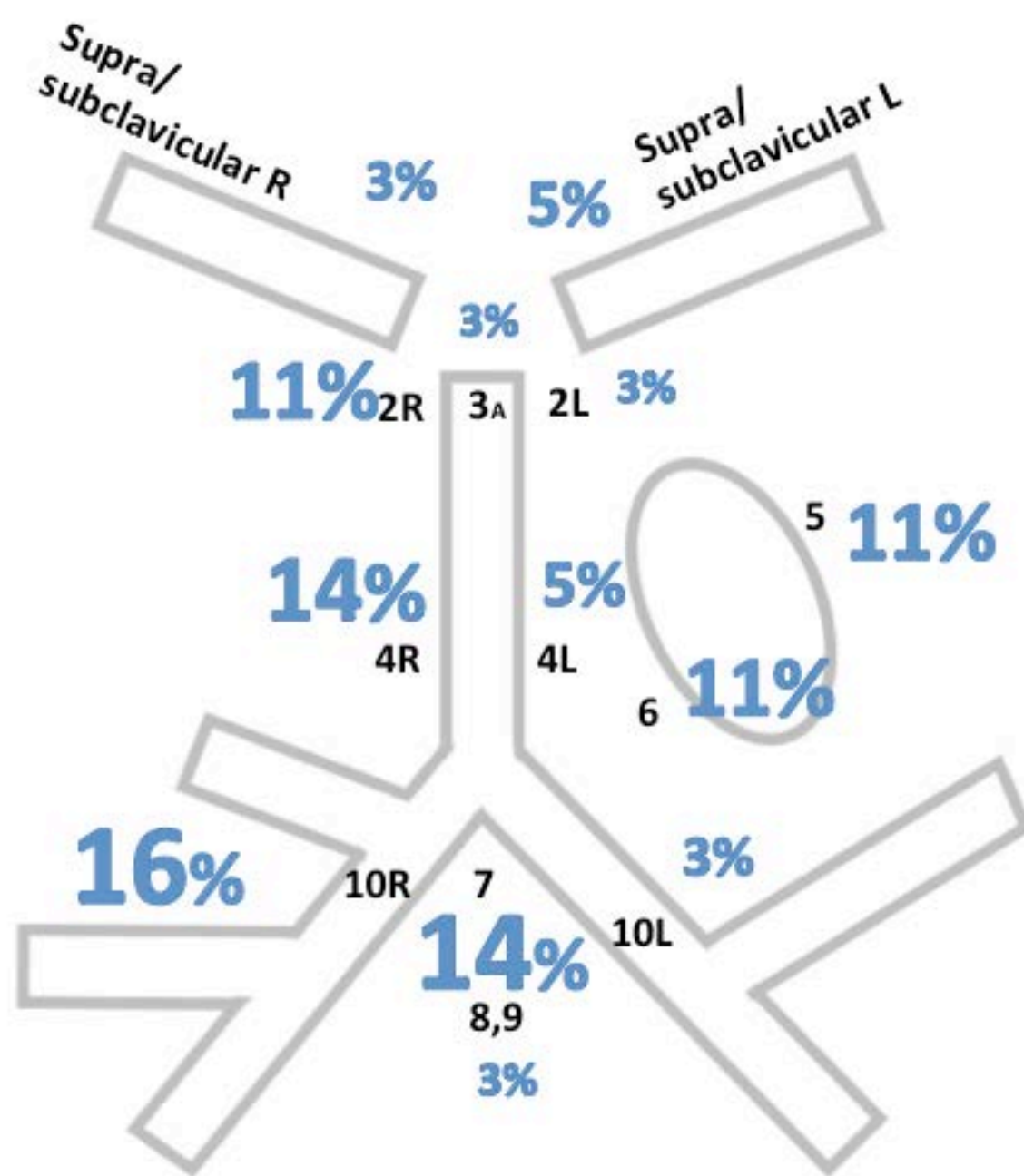
A) All LR patients (N=58)



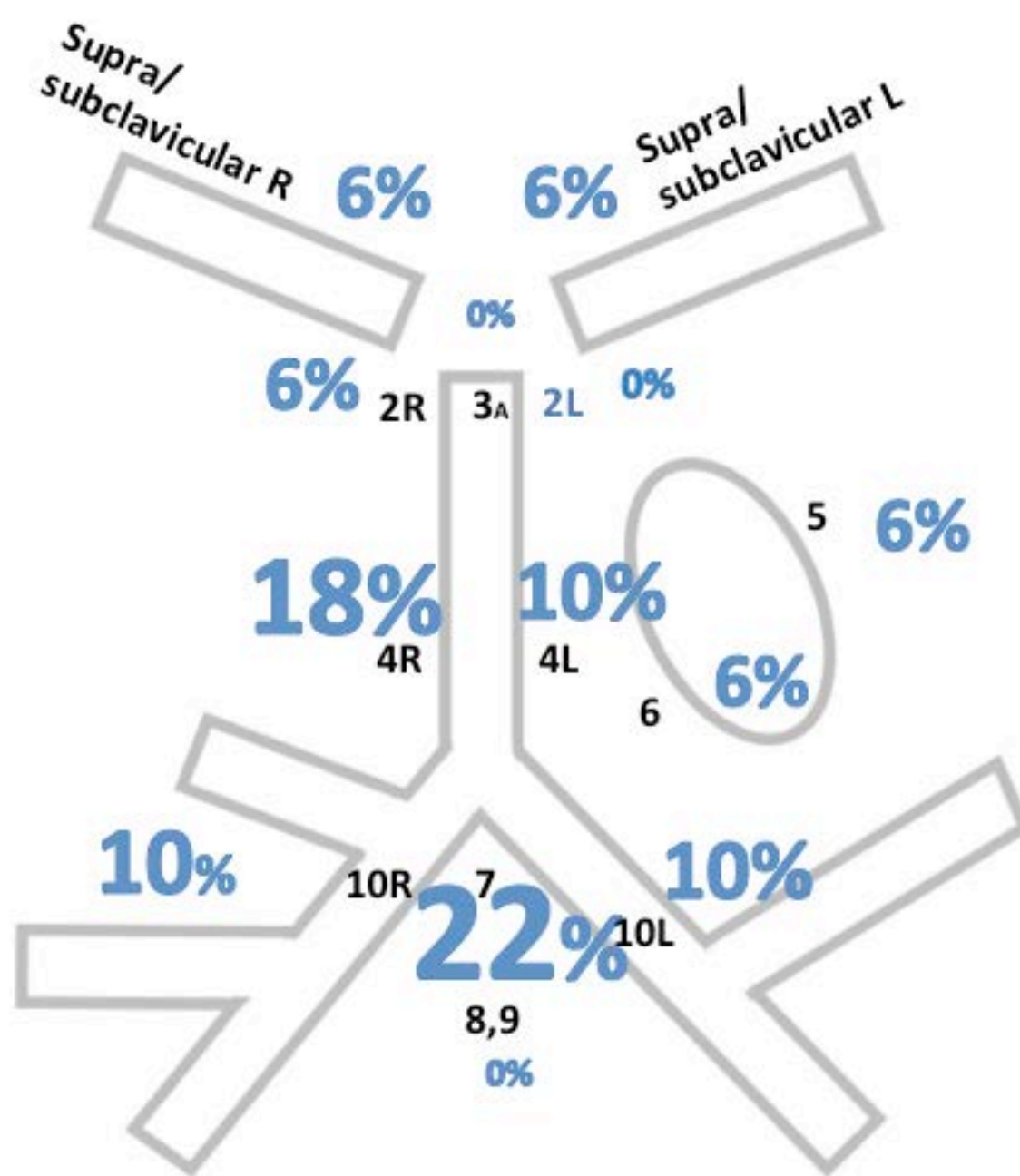
B) Right-sided tumors (N=42)



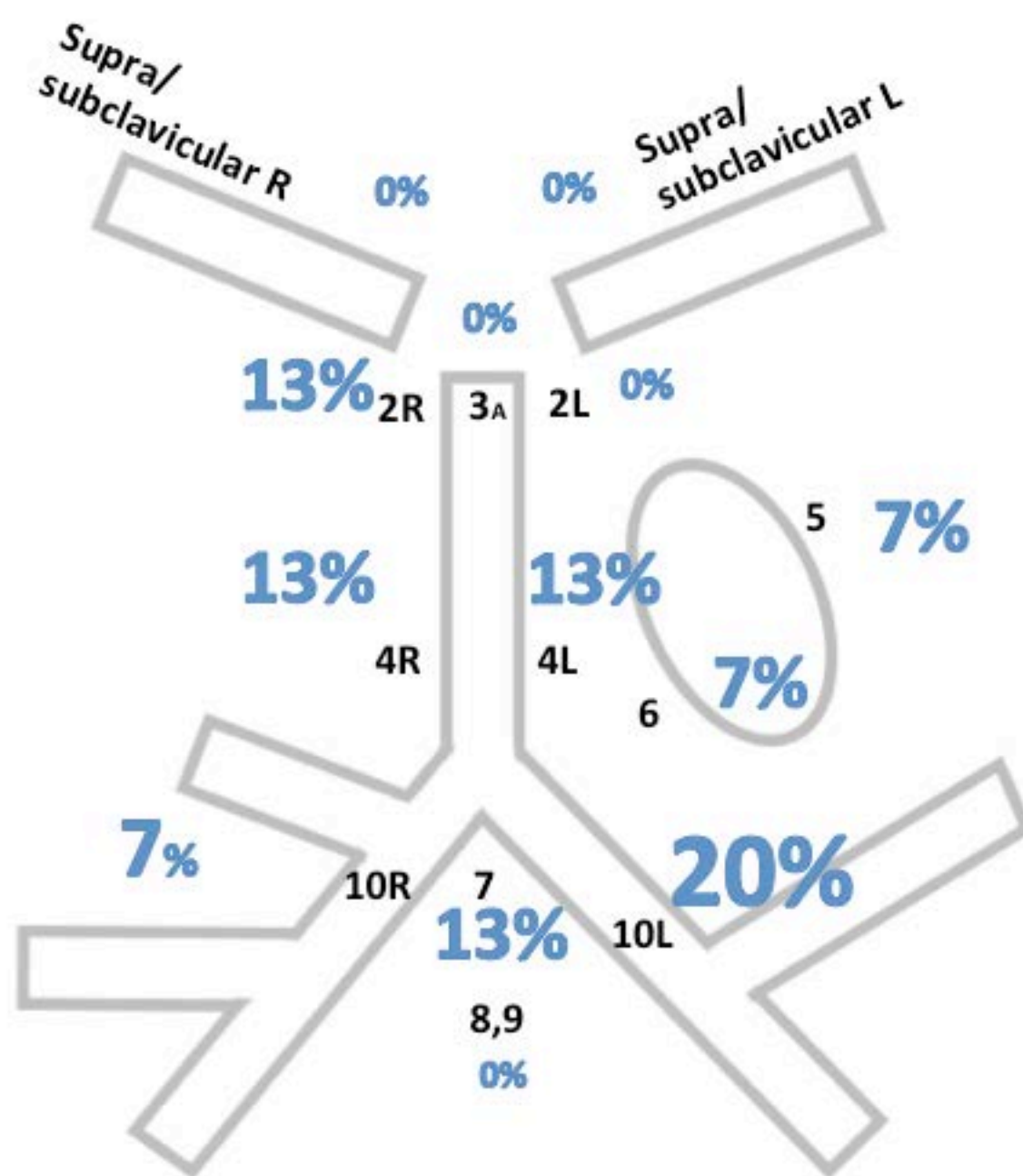
C) Upper and middle right-sided tumors (N=29)



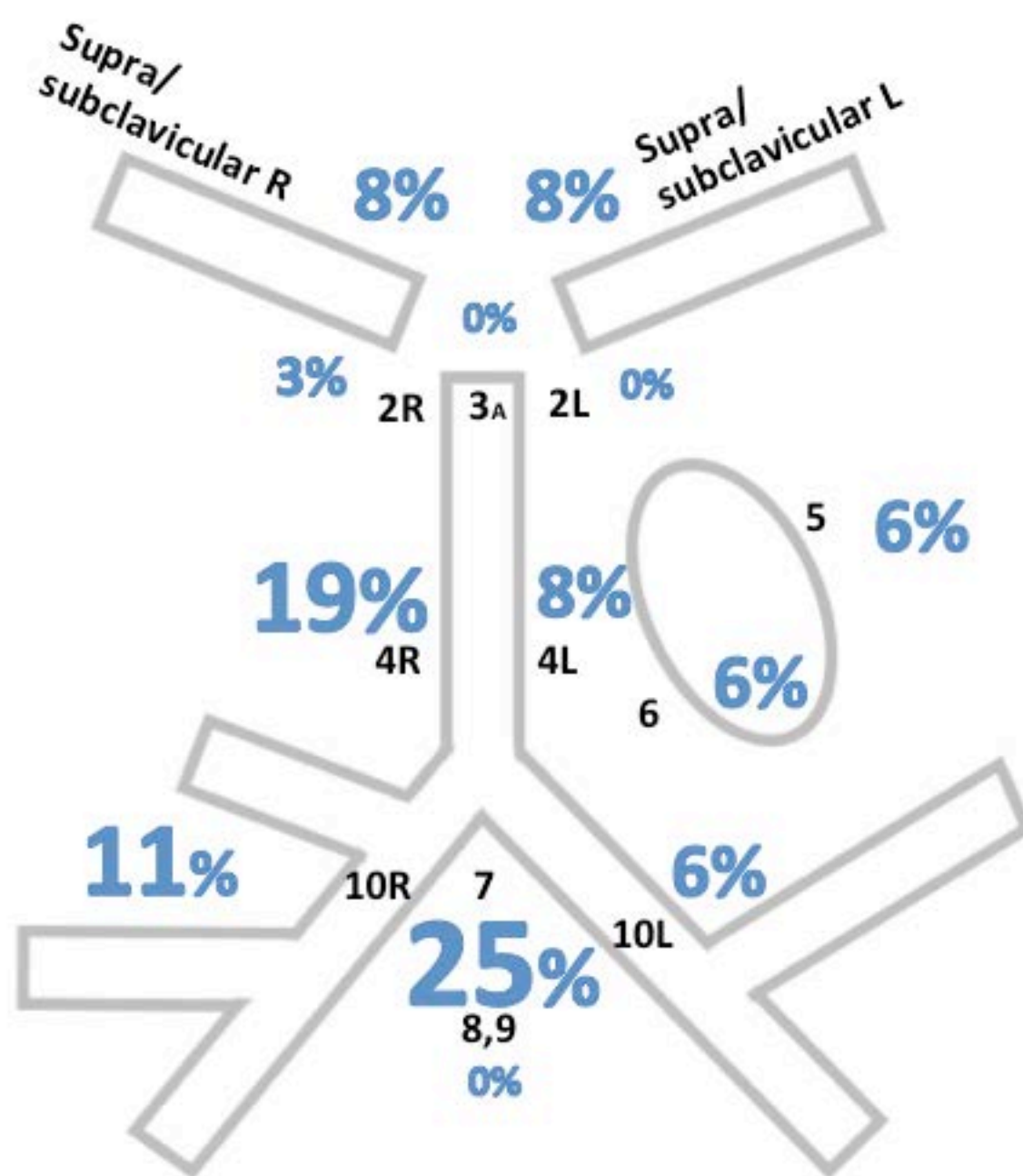
D) Lower right-sided tumors (N=13)



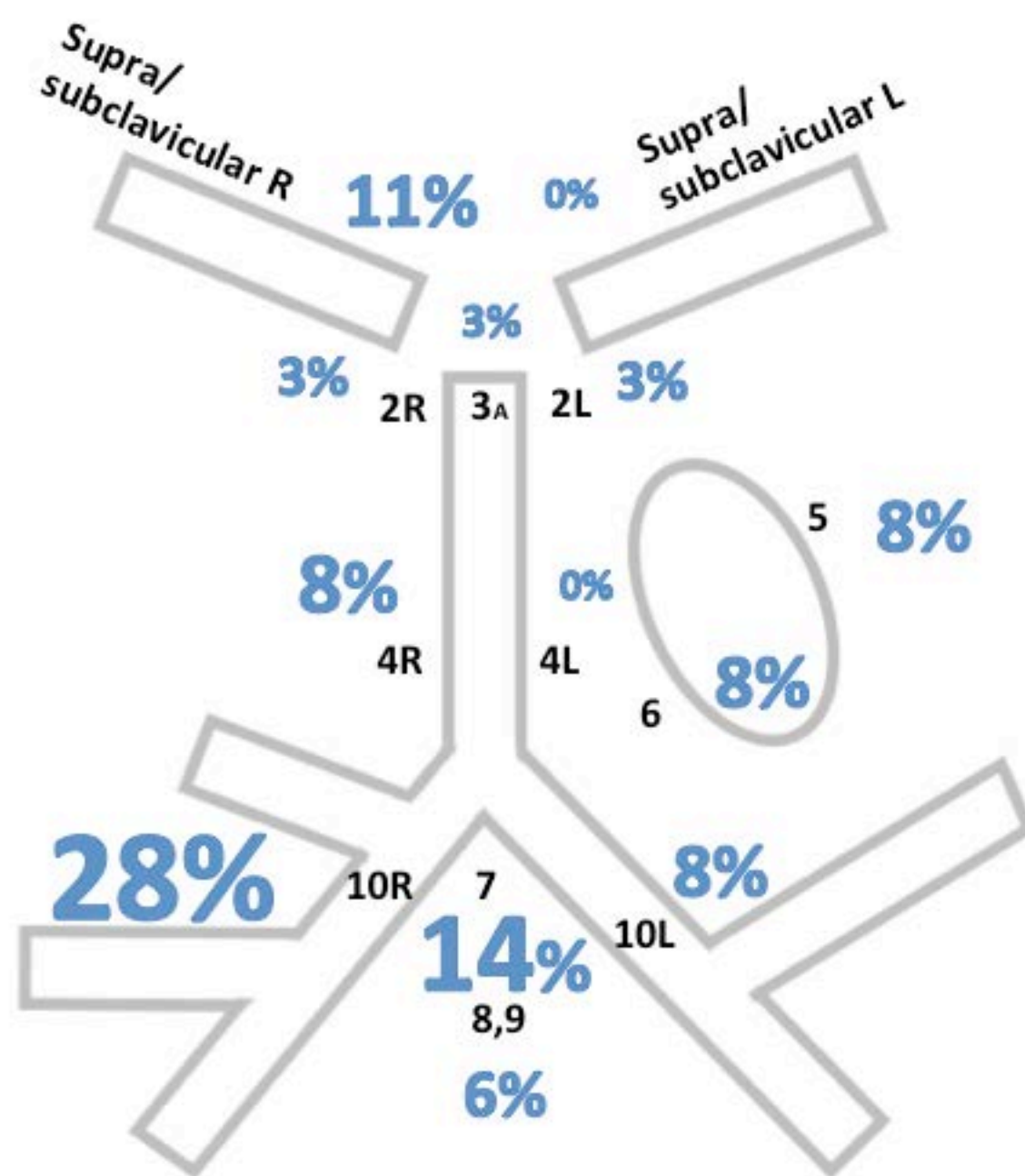
E) Left-sided tumors(N=16)



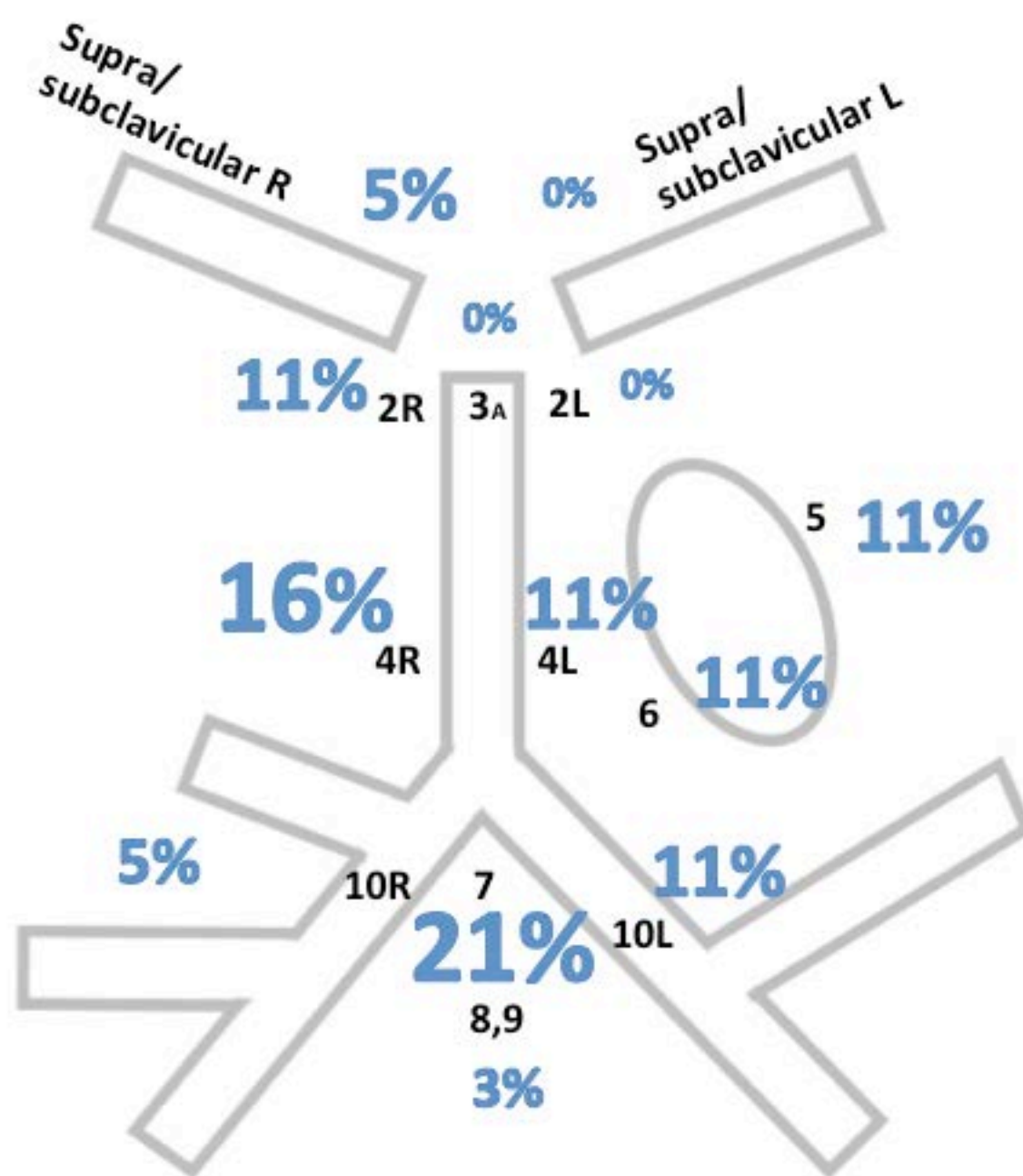
F) Upper and middle left-sided tumors (N=16)



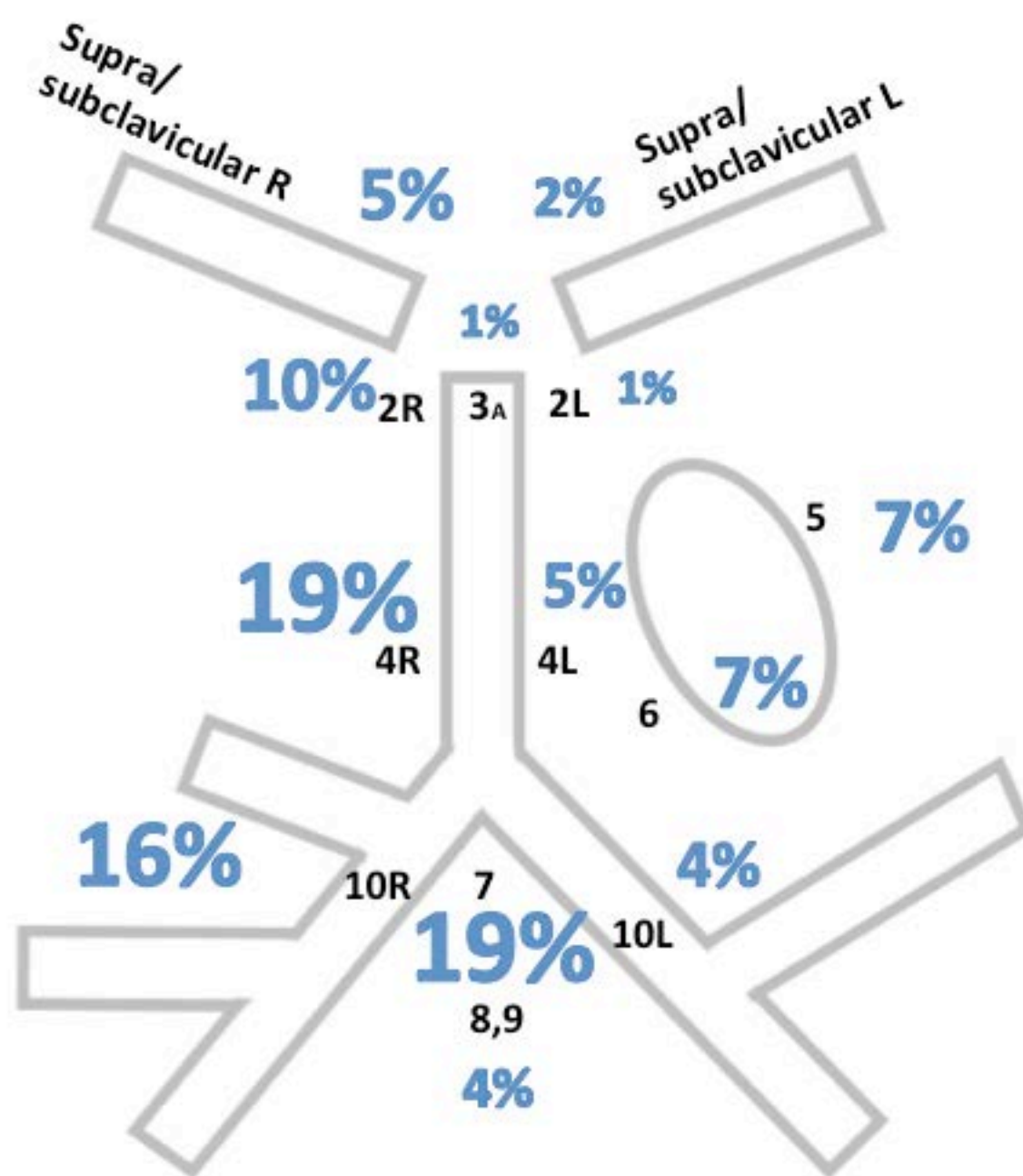
G) Lower left-sided tumors (N=10)



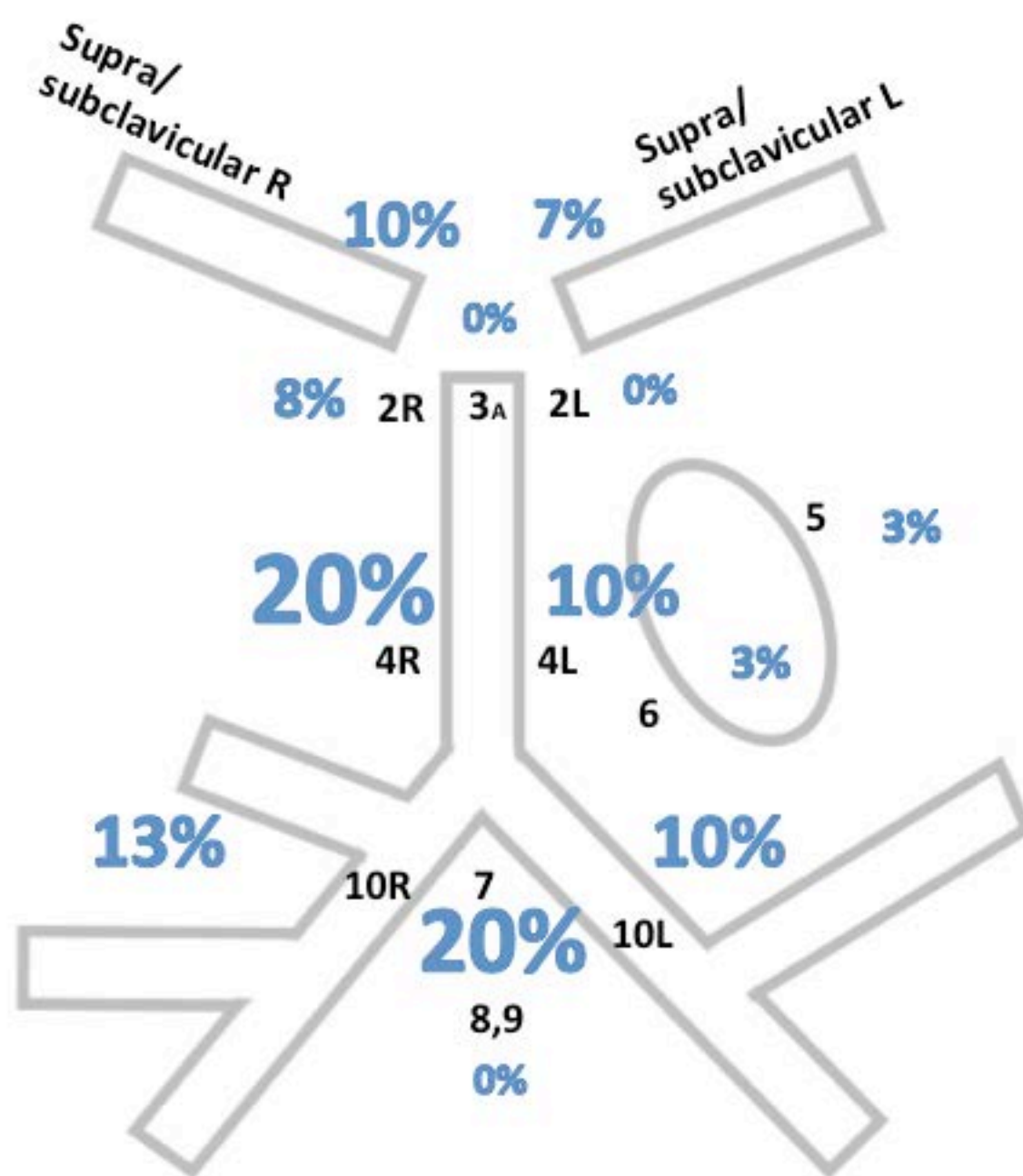
A) PORT group right-sided tumors (N=17)



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

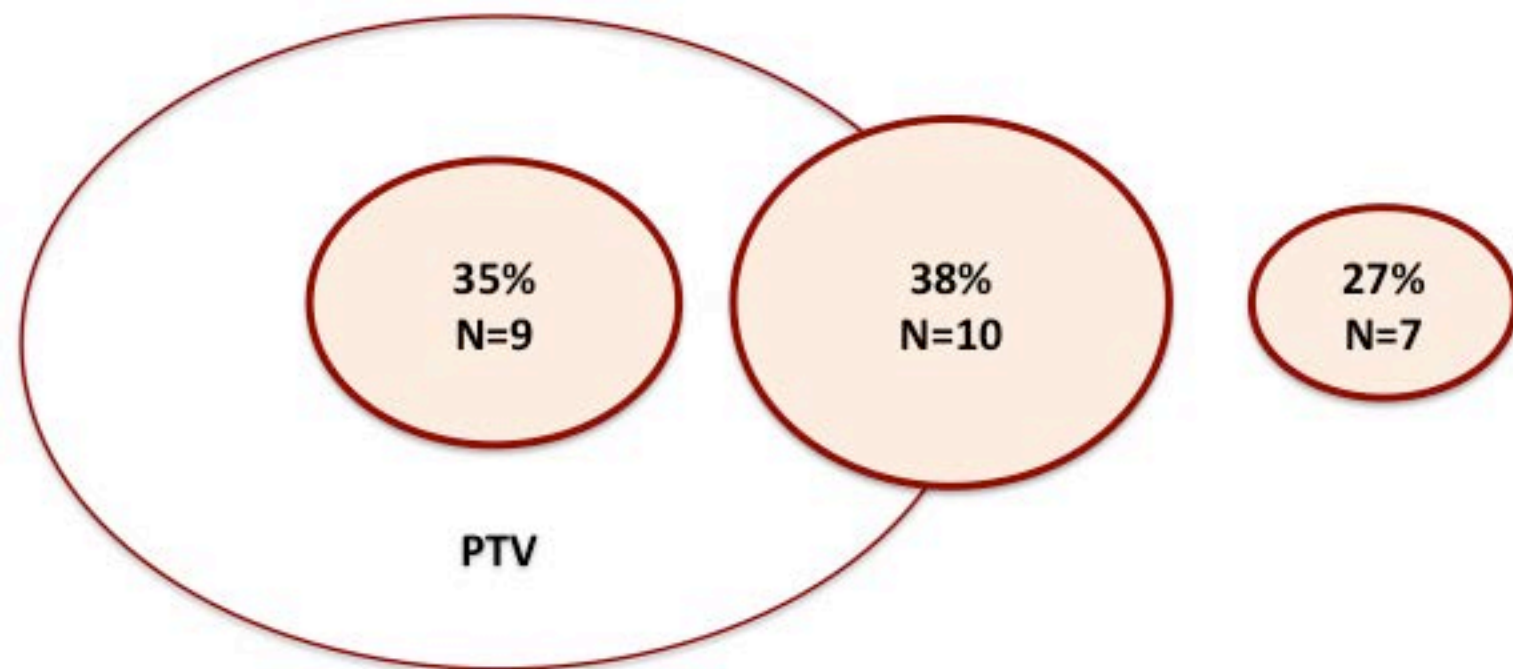


C) non-PORT group right-sided tumors (N=25)



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

A. PORT group (N=26)



B. Non-PORT group (N=32)

