

## Archaic and Capacious-Non Small Cell Carcinoma Lung

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Non small cell carcinoma lung is a pulmonary epithelial carcinoma disparate from small cell carcinoma lung. Majority (85%) of pulmonary malignancies are comprised of non small cell carcinomas.

Non small cell carcinoma is comprised of adenocarcinoma, squamous cell carcinoma or large cell carcinoma. Infrequently, subtypes such as pleomorphic carcinoma, carcinoid tumour, salivary gland carcinoma, unclassified carcinoma or uncommon, histological variants as mixed cell subtype may emerge [1, 2].

Exceptionally, pulmonary malignancies are comprised of an admixture of small cell and non small cell carcinoma, thereby designated as 'combined small cell carcinoma' lung [1, 2].

Cigarette smoking contributes to emergence of lung cancer by inducing injury to deoxyribonucleic acid (DNA). Residual, unrepaired DNA engenders non small cell carcinoma lung [1, 2].

DNA replication with genomic mutations, restored breaches within double-stranded DNA and augmented, inaccurate or deficient DNA restoration initiates excessive chromosomal mutation within pulmonary epithelial cell. Carcinomatous cells can exemplify > 100,000 mutations per genome [1, 2].

Epigenetic alterations and gene silencing of DNA repair genes is frequent. Commonly, DNA repair genes are repressed with promoter hyper-methylation [1, 2].

Exposure to radon, asbestos, chromium, nickel, beryllium, soot, tar, passive smoking, environmental pollution and family history of lung cancer predispose to disease emergence [1, 2].

Non small cell carcinoma lung exhibits a concurrence of chronic clinical symptoms. Preliminary disease enunciates hoarseness, chronic cough, haemoptysis, dyspnoea, anorexia, wheezing, chest pain or loss of weight [1, 2].

Advanced disease exhibits central nervous system manifestations as headache, weakness, dizziness, postural imbalance, seizures, jaundice, subcutaneous nodules, Pancoast's syndrome, numbness of extremities, bone pain or hypercalcemia with consequent nausea, vomiting or constipation [1, 2].

Cancer progression delineates occurrence of dyspnoea, dysphagia, superior vena cava syndrome, oedema of face or neck, persistent, repetitive infections as bronchitis or pneumonia, copious secretion of mucus, weakness, fatigue or hoarseness [1, 2]. [https://en.wikipedia.org/wiki/Non-small-cell\\_lung\\_carcinoma](https://en.wikipedia.org/wiki/Non-small-cell_lung_carcinoma) - cite\_note:-:2-15.

Pulmonary adenocarcinoma preponderantly occurs in peripheral pulmonary tissue, accounts for ~40% of lung carcinomas and is commonly discerned in non smokers [1, 2].

Squamous cell carcinoma lung appears as a centric neoplasm, depicts a male predominance and is commonly associated with cigarette smoking. Large cell carcinoma lung is a heterogeneous coterie comprised of undifferentiated, malignant neoplasms engendered

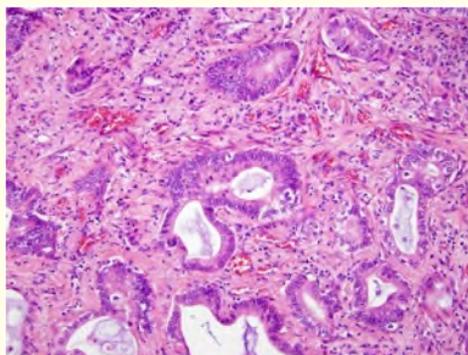
from transformed pulmonary epithelial cells [1, 2].

'Classic' large cell carcinoma lung is preponderantly constituted of poorly differentiated squamous cell carcinoma or adenocarcinoma [1, 2].

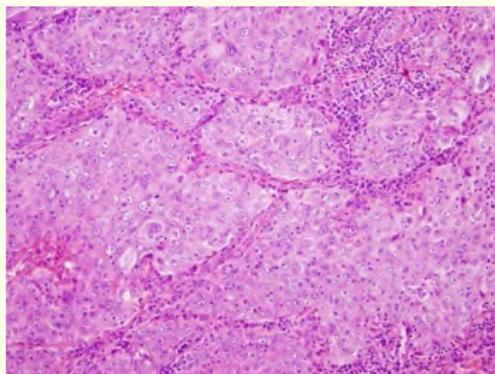
Cogent classification of the neoplasm as a small cell carcinoma, squamous cell carcinoma, adenocarcinoma or specific histological variants upon light microscopy may be challenging [1, 2].

Large cell carcinoma lung is composed of enlarged, anaplastic cells with enhanced nucleo-cytoplasmic ratio and an absence of "salt-and-pepper" chromatin, characteristically discernible in nuclei of small cell carcinoma [1, 2].

Non small cell carcinoma 'not otherwise specified' (NOS) is designated as such on account of minimally cellular or miniature tissue samples [1, 2].



**Figure 1:** Non small cell adenocarcinoma lung demonstrating glandular configurations layered with neoplastic, stratified and pseudostratified epithelium with cellular and nuclear atypia, pleomorphism and mitotic figures enmeshed within a fibrous stroma with red cell extravasation [5].



**Figure 2:** Non small cell carcinoma lung delineating nests of enlarged cells with altered nucleo-cytoplasmic ratio, abundant cytoplasm, vesicular nuclei and absent intercellular bridges. Mitotic activity, anaplasia and pleomorphism is prominent [6].

Staging of non small cell carcinoma lung is adopted in order to determine categorization and neoplastic differentiation along with possible therapeutic strategies [3, 4].

*Non small carcinoma lung is categorized into*

- Preliminary, non-metastatic disease constituted of stage I, stage II and pertinent stage III neoplasms
- Locally advanced disease confined to thoracic cavity as encountered with enlarged lesions, tumours implicating thoracic viscera or incriminated mediastinal lymph nodes
- Tumefaction with distant, extra-thoracic malignant metastasis [3, 4].

<b>Tumour</b>	<b>Node</b>	<b>Metastasis</b>
TX: Tumour cannot be assessed	NX: Lymph nodes cannot be assessed	
Tis: Tumour confined to superficial epithelial layers		
T0: No evidence of primary tumour	N0: Tumour deposits in regional lymph nodes are absent	M0: Distant metastasis are absent
<ul style="list-style-type: none"> <li>•T1mi: Minimally invasive adenocarcinoma of 3 cm with deep tissue invasion <math>\sim\frac{1}{2}</math> cm</li> <li>•T1a: Tumour <math>\sim</math>1cm, extension into visceral pleura or main bronchi absent</li> <li>•T1b: Tumour between 1cm to 2cm, extension into visceral pleura or main bronchi absent</li> <li>•T1c: Tumour between 2cm to 3cm, extension into visceral pleura or main bronchi absent</li> </ul>	N1: Tumour extends to intrapulmonary or ipsilateral hilar lymph nodes	<ul style="list-style-type: none"> <li>•M1a: Tumour extends to contralateral lung, malignant pleural effusion or malignant pericardial effusion</li> <li>•M1b: Single metastatic tumour nodule to distant sites as liver, bones, brain</li> <li>•M1c: Multiple metastatic tumour nodule to distant lymph nodes, liver, bones, brain</li> </ul>
<ul style="list-style-type: none"> <li>•T2a: Tumour between 3cm to 4cm, extends to visceral pleura or main bronchus, is 2cm away from carina or partially obstructs airways</li> <li>•T2b: Tumour between 4cm to 5cm, extends to visceral pleura or main bronchus, is 2cm away from carina or partially obstructs airways</li> </ul>	N2: Tumour extends to retro-tracheal or ipsilateral mediastinal lymph nodes	
T3: Tumour between 5cm to 7cm, extends to chest wall, parietal pleura, phrenic nerve, parietal pericardium or multi-focal tumour nodules within a single pulmonary lobe	N3: Tumour extends to ipsilateral or contralateral supraclavicular, hilar or mediastinal lymph nodes	
T4: Tumour >7cm, extends to carina, heart, mediastinum, aorta, trachea, oesophagus, diaphragm or vertebral column or depicts multi-focal tumour nodules within different pulmonary lobes		

**Table 1:** TNM classification of non small cell carcinoma [1, 2].

Cogent therapy is contingent to cancer stage, general health and age of incriminated subject, response to chemotherapy and accompanying side effects [3, 4].

Non small cell carcinoma lung is rather unresponsive to chemotherapy or radiotherapy [3, 4].

Preliminary non small cell carcinoma is optimally subjected to and alleviated with surgical pulmonary resection [3, 4].

Miniature, inoperable tumefaction can be treated with targeted radiotherapy with contemporary techniques as cyber-knife or stereotactic body radiation therapy [3, 4].

Percutaneous ablation and chemoembolization can be employed for treating non small cell carcinoma lung with techniques such as radiofrequency ablation (RFA), cryo-ablation and microwave ablation [3, 4].

Ablative techniques are efficacious in treating peripheral tumefaction or individuals unfit for surgery due to comorbidities or limited pulmonary function. Also, radiofrequency ablation followed by radiation therapy may depict enhanced survival on account of dual synergistic mechanisms of cell destruction [3, 4].

Palliation with pain relief is opted for treating advanced non small cell carcinoma lung. Palliation of tumour-induced clinical symptoms or tumour reoccurrence can be achieved with aforesaid thermal ablative techniques [3, 4].

Preoperative, neoadjuvant chemotherapy or postoperative adjuvant chemotherapy can be beneficially employed. Adjuvant or ancillary chemotherapy with platinum-based agents as cisplatin, carboplatin or combined chemotherapy with cetuximab or contemporary, targeted agents can be adopted [3, 4].

Genetic mutations of epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) can aptly guide pertinent therapy. Mutated genomic markers as BRAF, HER2/neu and KRAS are expressed which can regulate therapy [3, 4].

Non smokers with non small cell adenocarcinoma lung delineating drug-sensitizing mutations of epidermal growth factor receptor appear sensitized to medications as tyrosine kinase inhibitors comprised of erlotinib, gefitinib, afatinib or Osimertinib [3, 4].

Tumefaction with EML4-ALK translocation or mutation within ROS1 gene can be optimally managed with ALK inhibitors as crizotinib.

Advanced neoplasms devoid of EGFR or ALK mutations can be administered monoclonal antibody against vascular endothelial growth factor (VEGF) bevacizumab [3, 4].

Combined bevacizumab with carboplatin and paclitaxel adopted for reoccurring or advanced stage IIIB or stage IV disease can augment overall survival and progression-free survival [3, 4].

Tumour cells displaying programmed death-ligand 1 (PD-L1) can be treated with anti PD-L1 monoclonal antibody atezolizumab or anti programmed death receptor 1 (PD-1) monoclonal antibodies nivolumab and pembrolizumab or monoclonal antibody against cell surface Cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) ipilimumab [3, 4].

Immunotherapy with pembrolizumab is advantageous in treating metastatic, non mutating non small carcinoma lung where tumour cells expound PD-L1. The molecule can be utilized as a second line agent following failure of chemotherapy [3, 4].

Mobocertinib is indicated for locally advanced or metastatic non-small cell carcinoma lung demonstrating epidermal growth factor receptor (EGFR) mutations following disease progression upon platinum-based chemotherapy [3, 4].

Combined small cell carcinoma lung is generally subjected to therapeutic regimens akin pure small cell carcinoma lung [3, 4].

5 year proportionate survival decimates significantly with advanced disease. Stage I exhibits 5 year survival at ~47% whereas survival at stage IV is ~1% [3, 4].

Prognostic outcomes are significantly ameliorated with induction of immunotherapy [3, 4].

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5. Image 1 and 2 Courtesy: Cancer therapy advisor.

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