# Clinical Brief: Lung Cancer

June 2020

By Dr. Liana Romero, Siemens Healthineers GmbH
Prof. Dr. Wieland Voigt, Steinbeis-Hochschule Berlin GmbH

## Introduction

Lung cancer is the most commonly diagnosed cancer (11.6% of the total cases) and the leading cause of cancer death (18.4% of the total cancer deaths) among men and women combined.[1] Histologically, lung cancer is categorized into two presentations: non-small cell lung cancer (NSCLC) representing 70-80% of cancers and small cell lung cancer (SCLC) accounting for the remaining 20-30% of the more aggressive cancer presentation.[2] NSCLC cancers have been routinely sub-categorized into adenocarcinoma, squamous cell carcinoma and large cell carcinoma based on histological criteria. However, the histopathology of lung cancer has recently been re-classified by the World Health Organization (WHO) based on the growing volume of molecular profiles and genetic mutations such as EGFR and EML4-ALK fusion, thereby re-categorizing many large cell carcinomas as neuroendocrine tumors.[3]

Majority of the lung cancer patients (approx. 80%) are clinically symptomatic and present with cough, hemoptysis, dyspnea, chest pain, and non-resolving pneumonia.[4] Some may present with features suggestive of metastatic disease like skeletal pain or neurological symptoms and signs; however, less than 10% of the patients are fully asymptomatic when the cancer is detected as an incidental finding.[4] Factors such as age, gender, lung function, genetics, comorbidities, and environmental carcinogens play a role in predisposition and/or in prognosis, but early stage versus advanced stage detection is critical for favorable outcomes. NSCLC identified early (stage I) as a small, localized tumor and followed by surgical resection offers a 70-90% 5-year survival rate.[5,6,7] Unfortunately, over 75% of patients are at an advanced stage (stage III or IV) when diagnosed.

## Lung Cancer Screening and Diagnosis

The goal for improving prognosis of lung cancer is to detect the cancer at an early stage when treatment is more likely curative. Optimal delivery of lung cancer screening requires the targeting of those individuals most at risk. Established environmental risk factors for lung cancer include smoking cigarettes or other tobacco products, exposure to second-hand tobacco smoke, occupational lung carcinogens, radiation, and indoor and outdoor air pollution.[10] The first seminal study on lung cancer screening, the National Lung Screening Trial (NLST), showed that the use of low-dose chest computed tomography (CT) to screen high risk patients resulted in 20% lower mortality from lung cancer.[6,11] Most recently, the Dutch–Belgian lung-cancer screening trial (Nederlands–Leuvens Longkanker Screenings Onderzoek [NELSON]) showed that use of CT screening resulted in lower mortality rates of 24% in men and 33% in women.[11]

Most nodules or masses detected in the lung cannot immediately be identified as benign or malignant. However, the availability of artificial intelligence (AI) powered algorithms provides a tool to aid in increasing the proportion of nodules detected and correctly characterized via segmentation (measurement and volume).[13] AI has the potential to dramatically increase the efficiency, reproducibility, and quality of tumor measurements with automated segmentation.[14]

Once detected and initially characterized, further diagnostic testing is usually necessary to confirm malignancy, especially prior to a surgical intervention. The initial clinical staging using the tumor, node, and metastases (TNM) staging must be carried out in order to predict prognosis, dictate treatment modalities, and provide a standardized description of the disease.[15] Clinical staging may employ non-surgical means such as additional CT scans, radio-labeled 18fluorodeoxyglucose (18F-FDG) tumor cells with combined PET-CT or magnetic resonance imaging (MRI) to determine metastasis to the brain or other areas. A more recent addition is the application of "liquid biopsy" executed through the testing of tumor biomarkers in blood such as microRNAs.[6] Invasive staging procedures include tissue examination gained through fiberoptic bronchoscopy needle biopsy (often extended by endobronchial ultrasound) or transthoracic CT guided core needle biopsy.[15] Here again, the use of AI powered algorithms can facilitate characterization by staging tumors into predefined groups based on differences in appearance and spread that are important in determining the treatment strategies.[14]

Surgical-pathological staging represents the results of histology for all the specimens obtained during surgery, most commonly in NSCLC. It involves the tumor, and hilar and mediastinal lymph nodes from different sites obtained either by taking samples or by complete excision. The result represents the true stage of the cancer and is used to plan further therapy.[15] For patients with metastatic disease, the molecular pathology of the cancer cells is critical for the optimal selection of targeted therapy.

## Lung Cancer Therapy

The course of therapy is based on initial clinical stage, surgical-pathological stage, and the physiological status of the patient. The patient's physiological condition can be a factor in complications that may arise during therapy and/or the disease prognosis. Low-dose CT scans of the chest coupled with AI algorithms may aid in identifying underlying conditions by highlighting, segmenting and/or measuring other abnormalities in the lung such as emphysema and fibrosis. Additionally, low-dose CT scans can identify disorders of other organs. Examples include coronary calcifications, aortic aneurysms, nodules in the thyroid adrenals, adenopathy, liver and kidney disease, osteoporosis determined from bone density measurements, and vertebral body fractures.[16] Prevalence of these incidental findings have been reported to be as high as 59–73% in patient's scanned, with clinically significant findings present in approximately 14% of those cases.[17]

Main options for therapy include surgery with or without (neo)adjuvant chemotherapy, radiation therapy (external beam radiation therapy [EBRT]/stereotactic radiation therapy [SBRT]) either alone or in combination with chemotherapy or palliative chemotherapy, targeted therapy or immunotherapy.[12] However, lung cancer therapy is currently revolutionized due to the introduction of a large variety of new diagnostic and treatment options such as molecular diagnostics using next generation sequencing (NGS) or novel therapys such as stereotactic body radiation therapy (SBRT), interventional treatments, minimally invasive surgical treatment or several new targeted agents and immunotherapy with check point inhibitors.

 

## Guidelines for Therapy and Management

International and national guidelines for the management of lung cancer have been developed to promote evidence-based decision-making for increased quality of care, efficacy and standardization of treatment. Though compliance to guidelines is recommended, the overall compliance rate is often not satisfactory with studies showing adherence rates ranging from 33 to 61%.[18] Reasons for non-adherence may range from physicians defaulting to follow guidelines with which they are more familiar, option to use professional judgement, or complexity in accessing or interpretting.[18] Because of the sheer amount of studies, scientific evidence in oncology is rapidly evolving and treatment recommendations in guidelines are frequently adjusted to keep them up to date. However, for the individual physician, it may not be feasible to stay current in the ever-evolving field of lung cancer therapy and disease management.

For these reasons, multidisciplinary expert tumor boards (MDT) were established with core members from pulmonology, thoracic surgery, radiation oncology, medical oncology, radiology, nuclear medicine and pathology. The MDT has a high value in collaborative care, this based on the latest evidence to enforce the adherence to guidelines, to ensure timely decision-making and to educate trainee doctors. Like in other malignancies, disease management by the MDT becomes more patient centric – a trend that is reflected by the development of multidisciplinary clinics. Additionally, the MDT and the individual physician are now able to leverage AI powered solutions that facilitate access to guidelines and recommendations for therapy based on algorithmic evaluation of the patient's health history, cancer diagnosis, and personal preferences for treatment. This setting fosters the ideal physician-patient relationship and places the patient at the center of the decision-making.

## Conclusion

Lung cancer, while certainly a disease that currently has a high mortality, has been shown to have positive long-term prognosis when caught in the early stages. Low-dose chest CT screening provides a mechanism for screening that has been shown to aid in the early detection of the disease among high-risk patients. Additionally, it is important to recognize that the complement of AI in lung cancer screening performs three main clinical tasks: aiding in the detection, characterization, and monitoring of tumors.

### Guideline Adherence

Use of guidelines for lung cancer management promote evidence-based decision-making for increased quality of care, efficacy and standardization of treatment.

# References


1. Bray, F. et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *ACS Journal*, 12 September 2018. doi: 10.3322/caac.21492
2. Inamura, K. Lung cancer: Understanding its molecular pathology and the 2015 WHO classification. *Front Oncol*. 2017; 7: 193 doi: 10.3389/fonc.2017.00193
3. Travis W.D. et al. WHO Classification of Tumours of the Lung, Pleura, Thymus and Heart. *J Thorac Oncol*. 2015. doi: 10.1097/JTO.0000000000000663
4. Buccheri G, Ferrigno D. Lung cancer: Clinical presentation and specialist referral time. *Eur Respir J.* 2004;24:898–904. doi: 10.1183/09031936.04.00113603
5. Thomas A. et al. Trends and characteristics of young non-small cell lung cancer patients in the United States. *Front Oncol*. 2015;5:113 doi: 10.3389/fonc.2015.00113
6. Knight, S.B. et al. Progress and prospects of early detection in lung cancer. *Open Biol*. 2017 Sep; 7(9): 170070. doi: 10.1098/rsob.170070
7. Goldstraw P, et al. 2016. The IASLC lung cancer staging project: proposals for revision of the TNM stage groupings in the forthcoming (eighth) edition of the TNM classification for lung cancer. *J. Thorac. Oncol.* 11, 39–51. doi:10.1016/j.jtho.2015.09.009
8. Walters S, et al. 2013. Lung cancer survival and stage at diagnosis in Australia, Canada, Denmark, Norway, Sweden and the UK: a population-based study, 2004–2007. *Thorax*. 68, 551–564. doi:10.1136/thoraxjnl-2012-2022
9. Bannister, N. and Broggio, J. 2016. Cancer survival by stage at diagnosis for England (experimental statistics): Adults diagnosed 2012, 2013 and 2014 and followed up to 2015. https://www.ons.gov.uk
10. Alberg, A.J. et al. Epidemiology of lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest*. 2013 May;143(5 Suppl):e1S-e29S. doi:1378/chest.12-2345
11. de Koning, H.J. et al. Reduced lung-cancer mortality with volume CT screening in a randomized trial. *New Engl J Med*. Feb. 2020; 382:503-513 doi: 10.1056/NEJMoa1911793
12. Tao, L. et al. Trends in the incidence, treatment, and survival of patients with lung cancer in the last four decades. *Cancer Manag Res*. 2019; 11: 943–953. doi: 10.2147/CMAR.S187317
13. Sánchez, M. et al. Management of incidental lung nodules <8 mm in diameter. J Thorac Dis. 2018 Aug; 10(Suppl 22): S2611–S2627. doi:10.21037/jtd.2018.05.86
14. Bi, W. L et al. Artificial intelligence in cancer imaging: Clinical challenges and applications. CA Cancer J Clin. 2019 Mar-Apr; 69(2): 127–157. doi: 10.3322/caac.21552
15. Koukis, I. et al. Clinical and surgical-pathological staging in early non-small cell lung cancer. Oncol Rev. 2013 Apr 22; 7(1): e7. doi: 10.4081/oncol.2013.e7
16. Midthun, D. E. Early detection of lung cancer. Version 1. F1000Res. 2016; 5: F1000 Faculty Rev-739. doi: 10.12688/f1000research.7313.1
17. Jacobs, P. et al. Prevalence of incidental findings in computed tomographic screening of the chest: A systematic review. Journal of Computer Assisted Tomography: March-April 2008 - Volume 32 - Issue 2 - p 214-221 doi: 10.1097/RCT.0b013e3181585ff2
18. Heins, M. J. Adherence to cancer treatment guidelines: influence of general and cancer-specific guideline characteristics. European Journal of Public Health, Volume 27, Issue 4, August 2017, Pages 616–620, doi: 10.1093/eurpub/ckw234



**Siemens Healthineers Headquarters**
Siemens Healthcare GmbH
Henkestr. 127
91052 Erlangen, Germany
Phone: +49 9131 84-0
siemens-healthineers.com



*Published by Siemens Healthcare GmbH · 0620 online · © Siemens Healthcare GmbH, 2020*