



**INTERNATIONAL JOURNAL OF
PHARMACEUTICAL SCIENCES**
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: <https://www.ijpsjournal.com>



Review Article

Advances in Lung Cancer: Diagnostics, Molecular Pathways, and Emerging Therapeutic Strategies

Ashok Bendgude*¹, Shubham Patil², Siddhi Shirahatti³, Disha Fartade⁴, Ajit Patil⁵, Anilkumar Shinde⁶

^{1,2,3,4,5} Tatyasaheb Kore College of Pharmacy, Warananagar, Tal Panhala, Kolhapur.

⁶ Bharati Vidyapeeth College of Pharmacy, Kolhapur.

ARTICLE INFO

Published: 11 May 2026

Keywords:

Lung cancer, NSCLC, SCLC, Nanoparticles, Targeted therapy, Immunotherapy, Drug delivery.

DOI:

10.5281/zenodo.20123652

ABSTRACT

Lung cancer is presently the leading cause of cancer-related mortality. It is observed worldwide because of its delayed identification, histological heterogeneity, and complex molecular aetiology with significant mutations in EGFR, ALK, KRAS, and TP53. Overall survival rates are still low despite advancements in traditional therapies including radiation, chemotherapy, and surgery, especially in cases of advanced cancer. Precision medicine techniques, such as immunotherapy, photothermal therapy, and molecular targeted therapy, are the focus of emerging therapeutic methods. With its targeted administration, improved bioavailability, controlled release, and less systemic toxicity, nanomedicine has attracted a lot of interest as a flexible platform for treating lung cancer. Exosomes, lipid nanoparticles, magnetic nanoparticles, polymeric nanoparticles, Liposomes and PLGA-based nanoparticles are two nanocarriers that have shown encouraging preclinical and clinical results. These approaches enhance anticancer efficacy while minimizing off-target effects by enabling the co-delivery of chemotherapeutics, nucleic acids, and gene-silencing agents. Therapeutic safety and selective targeting are further enhanced by functionalization with tumor-specific ligands and responsive polymers. This review highlights the potential of recent advancements in lung cancer immunotherapy, photothermal therapy, molecular targeted therapy, and nanocarrier-mediated drug delivery to address the shortcomings of conventional approaches and provide customized treatment regimens. Future studies should focus on enhancing nanoparticle design, assessing long-term safety, and translating preclinical results into clinical applications in order to improve patient outcomes.

INTRODUCTION

The term "cancer" refers to a group of around two hundred diseases that share comparable

*Corresponding Author: Ashok Bendgude

Address: Tatyasaheb kore college of pharmacy, Warananagar, Tal Panhala, Kolhapur.

Email ✉: ashokbendgude123@gmail.com

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.



characteristics rather than a single illness. Cancers (carcinomas) are characterised by unchecked cell growth and spread to other bodily areas(1).

The lymph nodes are frequently the primary location of lung cancer metastases in individuals. As a result, assessing lymph node involvement prior to surgery is crucial for choosing the best course of action. In order to look for tumor cells, lymph nodes are usually taken after surgery and inspected under a light microscope.

If tumour cells are found in the lymph nodes, patients are often recommended further chemotherapy. However, the spread of cancer to lymph nodes may go undetected due to the low sensitivity of existing clinical diagnostic methods, which could result in poor survival outcomes even after diagnosis. Consequently, more advanced and sensitive diagnostic methods are needed(2).

Like all malignancies, lung cancer is caused by acquired abnormalities in the cell, the fundamental building block of life. The body keeps its regulatory system in place. that govern cell growth and division under normal physiological conditions, making sure that new cells are only created when necessary(3).

Like all malignancies, lung cancer is caused by acquired defects in the cell, the fundamental building block of life. Under normal physiological settings, the body maintains a system of regulatory systems that control cell growth and division, ensuring that new cells are only produced when required(4).

Lung cancer is caused by a variety of genetic and epigenetic changes that impact important genes controlling the cell cycle(5).

These changes could build up in the bronchial epithelium and cause aberrant cells to proliferate

clonally. Clonal cell populations may also develop in histologically normal tissues next to malignancies in some patients. (6).

Additionally, some cancer patients have chromosomal abnormalities that either deactivate tumor suppressor genes or activate oncogenes. Chromosome regions such as 13q, which contains the RB gene; 17p, which contains the TP53 tumor suppressor gene; 9p, which contains the p16INK4a and p19ARF genes involved in the RB signaling pathway; and 3p, which contains the FHIT tumor suppressor gene, are frequently altered in lung cancer(7).

The epidemiology of lung cancer

One of the most frequently diagnosed malignancies and the primary cause of cancer-related death globally is lung cancer. With an anticipated 2.2 million new cases and 1.8 million fatalities recorded in 2020, it is thought to be responsible for around 18% of cancer-related deaths worldwide and nearly 11–12% of all new cancer cases, underscoring its substantial impact on global health.(8) About 85–90% of cases of lung cancer are caused by tobacco use. As a result, it is thought to have a significant role in the disease's progression. Secondhand smoking exposure, occupational carcinogens, air pollution, and genetic vulnerability are other important risk factors. The majority of people with lung cancer are 65 years of age or older(9).

Due to variations in smoking rates, environmental exposures, and socioeconomic factors, lung cancer incidence varies geographically throughout the world. Africa and South-Central Asia have comparatively lower incidence rates, while Eastern Asia, Europe, and North America have higher rates(10).



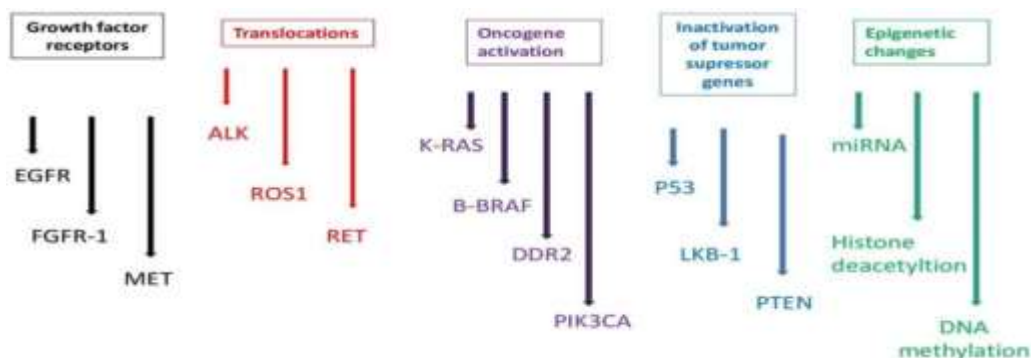
In order of priority, the following broad categories are applied to the approaches used to estimate cancer incidence rates by age and sex within a given country. In 45 countries, the observed national incidence rates were projected to 2018. The 2018 national or regional incidence rates were then applied to the populations of 50 countries. Using national mortality data and death-to-incidence ratios obtained from cancer registries in 14 countries, the rates were estimated through modeling. By applying modeling based on death-to-incidence ratios from cancer registries in neighboring countries (37 countries), the rates were derived from national mortality estimates. By averaging the overall rates from neighboring countries, the national incidence rates for all cancers combined, stratified by age and sex, were determined. Using the available cancer-specific relative frequency data from 7 countries, these rates were further divided to estimate the national incidence for each cancer site. Rates were also estimated by averaging data obtained from 32 neighboring countries.

When estimating future cancer incidence and mortality, careful consideration is required. Projections for upcoming years rely on key assumptions, as is the case with all estimation methods. One assumption is that during the projection period from 2020 to 2040, the national rates predicted in 2018 remain constant. Another

assumption is that the national population data for these years are accurate. However, gaps still exist in the availability and quality of cancer data worldwide, particularly in low- and middle-income countries. These estimates were generated using the methodology of the International Agency for Cancer Research, which extends beyond simply collecting, evaluating, and using data from its cancer registry partners and also includes collaboration with national personnel to enhance local data quality, registration coverage, and analytical capacity(11).

Pathophysiology of lung cancer

Lung cancer is a multifaceted, intricate molecular process. The molecular etiology of lung cancer includes a variety of biological events that contribute to the growth and metastasis of tumors (12). Lung cancer can arise due to a variety of genetic factors and epigenetic modifications. These alterations include chromosomal translocations, insertions, deletions, point mutations, and gene amplifications. The activation of carcinogenic pathways that promote unregulated cell division is intimately associated with these genetic and epigenetic changes (13). These alterations either restrict or eliminate tumor-suppressor pathways, which normally regulate cell division and death(14).



Molecular Biology of Lung Cancer

Recent bench and clinical research has improved lung cancer treatment by allocating medications



according to histology and molecular characteristics (15). Tyrosine kinase inhibitors targeting mutations such as When compared to traditional treatments, patients with adenocarcinoma bearing EGFR mutations have significantly higher response rates when using the Epidermal Growth Factor Receptor (EGFR) (16). The development of new targeted therapeutics requires a deeper comprehension of the molecular processes involved in tumor initiation and progression. Improving high-throughput biomarker discovery platforms and detecting molecular changes are essential for developing individualized treatment plans (17).

The primary cause of cancer-related death globally is still lung cancer. Comparing the total 5-year survival rate to other prevalent tumors, it is still low. One of the main causes of the high death rate from lung cancer is that the disease is frequently discovered at an advanced stage. The variation in lung cancer's biochemistry and histology is another factor (18). Non-small cell lung cancer used to be treated as a single illness. However, current therapeutic approaches distribute treatments according to molecular changes and histology. Patients with EGFR-mutated adenocarcinoma have shown better results with targeted therapy aimed at EGFR mutations(19).

Lung Carcinogenesis

Tumor initiation and progression involve multiple sequential molecular events including DNA damage induced by tobacco carcinogens(20). These events include field carcinogenesis in airway epithelium and the subsequent development of malignant tumors (21). Only a small percentage of smokers get lung cancer, despite tobacco use continuing to be the leading risk factor(22).

Mutations in Somatic DNA

Lung cancers have often been shown to have chromosomal abnormalities like deletions, translocations, and loss of heterozygosity. These genetic changes could be used as indicators for prognosis and diagnosis. The identification of somatic mutations in cancer genomes has significantly increased thanks to advancements in sequencing methods(23).

Early studies focused on sequencing individual genes such as TP53 and CDKN2A(24). Traditional Sanger sequencing has limitations in detecting low-frequency mutations. Large sequencing projects have identified numerous mutated genes involved in lung cancer development. Whole-genome sequencing now allows comprehensive identification of genomic alterations within tumors (25)

Pathways of Lung Development and Differentiation

According to current models, stem cells or pluripotent progenitor cells are the source of lung malignancies(26). Lung tumor signatures and embryonic lung development pathways are comparable, according to gene expression studies(27). Genes linked to early developmental pathways are often expressed in poorly differentiated cancers. Tumor aggressiveness and a poor prognosis are caused by these developmental gene pathways(28).

Gene Rearrangements and Copy Number Changes

Lung cancer is significantly influenced by chromosomal abnormalities, such as gene amplifications, deletions, and rearrangements(28). A common method for identifying chromosomal aberrations in lung cancer samples is fluorescence in situ hybridization (FISH). FISH has shown high sensitivity and specificity for detecting lung cancer



in bronchial washings and cytological samples(29). Certain non-small cell lung tumors harbor the EML4-ALK fusion oncogene; patients with this rearrangement respond well to targeted therapy with ALK inhibitors (30). Amplification of SOX2 has been observed in squamous cell lung carcinoma (31). Similarly, sensitivity to FGFR inhibitors has been linked to FGFR1 amplification(32).

Historical Classification of Lung Cancer

Determining the histologic type and molecular biomarkers is critical for proper patient therapy since it allows medicines to be adjusted according to tumor features(33). About one-third of lung cancers are surgically resectable when they are discovered early(34). In these situations, precise tumor categorization, staging, and prognostic factor assessment are made possible by pathological investigation of resected specimens(35). Nonetheless, over 70% of lung cancer cases are discovered when the tumors are too large to be removed. Small diagnostic samples, such as biopsy or cytology specimens, serve as the primary diagnostic tool in these cases. Consequently, the classification of lung cancer based on microscopic samples differs from that based on complete surgical resection specimens (36).

The pathologic diagnosis derived from biopsy specimens typically exhibits a high degree of diagnostic precision. However, certain biopsies could not yield a conclusive diagnosis because of things like tiny tumors or necrotic tissue(36). According to research, metastatic cancers frequently have diverse, site-specific genetic changes that could be linked to a more aggressive course of the illness(37). Therefore, biopsy of metastatic tumors may offer additional information on aggressive mutations along with histology and staging details. Radiologists play an

essential role in evaluating patients with lung cancer by detecting primary tumors, identifying metastatic disease, and selecting the most appropriate biopsy target(38).

Histological classification continues to be the most significant component in the detection and treatment of lung cancer. Patient outcomes have been greatly enhanced by developments in the knowledge of genetic alterations and the creation of targeted medicines. However, routine testing for immunological markers like PD-L1 (Programmed Death Ligand 1) and other driver mutations including ROS1, BRAF, NTRK, RET, KRAS, and MET is recommended by current clinical standards. Recent studies have also developed novel grading systems for invasive non-mucinous lung adenocarcinoma and classified multiple thoracic cancers (39).

Subclassification of Invasive Lung Adenocarcinoma

The invasive subcategories in the 2015 classification system for lung adenocarcinoma—minimally invasive adenocarcinoma, invasive non-mucinous adenocarcinoma, invasive mucinous adenocarcinoma, colloid adenocarcinoma, fetal adenocarcinoma, and enteric-type adenocarcinoma—remain largely unchanged(40). However, the most prevalent subtype of lung cancer, invasive non-mucinous adenocarcinoma, now features a revised grading system(40). The majority of lung adenocarcinomas that are surgically removed have a combination of histologic subtypes or architectural development patterns. Lepidic, acinar, papillary, solid, and micro papillary growth patterns are among them. Each tumor has a different percentage of these histologic patterns(41).

The major histologic subtype was used to define diagnostic and prognosis categorization in the



2015 WHO classification system. Lepidic-dominant tumors were categorized as either low-grade or well-differentiated(41). Strong correlations between this histologic classification system and clinical prognosis have been repeatedly shown. Studies indicate that even a small proportion of high-grade histologic patterns, such as solid, micropapillary, complex glandular, or cribriform forms, may be linked to poorer clinical outcomes(41).

Lung Cancer Staging

The next critical stage in the process from diagnosis to therapy is staging, which comes after the histologic type of lung cancer has been identified. Results from imaging methods like CT and PET scans, as well as tissue analysis from biopsy procedures, are used in staging. The staging process helps doctors determine each patient's best course of action(42).

Additionally, lung cancer staging is utilized to assess the disease's overall prognosis. Prognosis is generally estimated by comparing outcomes among patients with similar cancer types and stages. However, individual responses to treatment vary considerably, and predicting life expectancy in a specific patient remains challenging (43).

The staging process usually begins with evaluation of imaging findings and biopsy results before treatment initiation, allowing clinicians to assign a clinical stage. In certain patients, pre-treatment intranodal staging is recommended to determine whether lymph nodes within the chest are involved.(43) If surgical resection is performed as the first treatment, a pathological stage is assigned based on findings from the resected specimen. In cases where cancer recurs after treatment, restaging is typically performed using the same diagnostic techniques (44).

In contrast, small cell lung cancer (SCLC) has two stages: extensive stage and limited stage. One hemithorax and local lymph nodes are the only areas affected by limited-stage illness. Metastasis to distant organs or the contralateral lung is indicative of extensive-stage illness (15). Lung cancer treatment choices are heavily influenced by the patient's overall health, tumor subtype, and disease stage(41).

Clinical Presentation of Lung Cancer

Studies that evaluated diagnostic tests using histologic reference standards comprised at least 50 cases(45). The recommendations were developed and evaluated by the Lung Cancer Guideline Panel, the Board of Regents of the American College of Chest Physicians, and the Thoracic Oncology Network (46).

Sputum cytology is a reliable method of diagnosing lung cancer, with a combined specificity of 99% and sensitivity of 66%. Sensitivity is influenced by the tumor site; FB has an 88% sensitivity for central, endobronchial malignancies(47). The diagnostic yield for peripheral lesions is lower: lesions measuring less than 2 cm show a sensitivity of 34%, whereas those greater than 2 cm demonstrate a sensitivity of 63% (48). The diagnosis of peripheral lung lesions is improved by new methods like R-EBUS and EMN bronchoscopy, which give 73% and 71%, respectively(49).

TTNA has a 90% pooled sensitivity for lung cancer diagnosis, despite somewhat reduced sensitivity for tumors smaller than 2 cm.(50). When compared to bronchoscopic procedures, TTNA is linked to a greater risk of pneumothorax. Pleural fluid cytology has a mean sensitivity of approximately 72% in patients with malignant pleural effusions (50). Image-guided closed biopsy gives 75–88%, thoracoscopic biopsy



yields the best diagnostic yield at 95–97%, and closed pleural biopsy yields 38–47%(36).

Despite the clinical, pathological, and genetic diversity of NSCLC tumors, cytology can accurately distinguish SCLC from NSCLC. Over the past ten years, clinical trials have shown that NSCLC responds differently to treatments according on its molecular and histologic characteristics. In order to accurately characterize NSCLCs histologically and molecularly, doctors performing diagnostic procedures must guarantee adequate tissue acquisition (51).The sensitivity of bronchoscopy is weak for peripheral lesions less than 2 cm, but it is good for endobronchial illness. Although there is a higher risk of pneumothorax, TTNA sensitivity is great for malignant illness (46).The diagnostic yield for peripheral lung malignancies is increased by R-EBUS and EMN bronchoscopy. The most effective method for diagnosing metastatic pleural effusions is thoracoscopic pleural biopsy(51).

Diagnosis of Lung Cancer

This article revises earlier ACCP Lung Cancer Guidelines by adding fresh evidence on diagnostic methods as well as historical data(36).Data summaries were created to represent current best practices as new technology or processes were available. The impact on diagnostic processes is highlighted due to the increasing significance of differentiating NSCLC cell types for discovering genetic alterations(50).

Thoracentesis

Patients with pleural effusions suspected of lung cancer should undergo thoracentesis(55. Because malignant cells verify the pleura's metastatic participation, differentiating between malignant and paramalignant effusions is crucial from a therapeutic standpoint(38).

Diagnosis of Primary Tumor

To make a final diagnosis, a number of methods are available, including sputum cytology, flexible bronchoscopy (FB), EMN bronchoscopy, R-EBUS, and TTNA (52).When choosing a diagnostic modality, the primary objectives are to: (i) optimize diagnostic and staging yield; and (ii) prevent needless intrusive tests while taking the intended course of therapy into account(53).

Conclusion

Lung cancer can be definitively diagnosed using a range of diagnostic methods .. The optimal test should ideally be selected by a multidisciplinary team of radiologists, pathologists, thoracic surgeons, and pulmonologists(54).Tumor type (SCLC or NSCLC), tumor size and location, and the estimated cancer stage typically influence the test selection(54).

Early Lung Cancer Detection and Screening

Despite improvements in treatment, lung cancer remains incurable for many patients due to the advanced stage of diagnosis. Despite the fact that 70% to 80% of lung cancer cases Since lung cancer mostly affects former smokers, smoking bans would have the most effect on lung cancer mortality in the Western world. Early identification techniques include bronchoscopy in high-risk individuals, biomarkers, imaging screening (CT, chest X-ray), and public awareness of symptoms(55) .

CT Scan

Chest radiography was largely ineffectual in the early lung cancer screening trials carried published in the 1980s and 1990s.CT with low-dose multidetectors (LDCT) has been the focus of much study throughout the last 20 years(56).When it comes to identifying tiny, non-calcified, solitary



pulmonary nodules (SPNs), chest CT is more sensitive than radiography(57). Higher lung cancer detection rates, frequently at early and treatable stages (IA–IB), were seen in non-randomized LDCT investigations. Despite certain biases, studies like I-ELCAP showed extremely high 5- and 10-year survival rates for stage I lung malignancies(53).

National Lung Cancer Screening Trial (NLST)

The NLST was the first randomized controlled trial (RCT) to demonstrate that LDCT reduced lung cancer-specific mortality(58). In contrast to 6.9% in the radiography arm, approximately 24.2% of participants in the LDCT arm had a positive screen(59). There were high false-positive rates: 6.5% for radiography and 23.3% for CT. Adenocarcinoma accounted for 50% of the 1060 lung tumors found in the LDCT arm at stage I. In contrast, 31% of the 941 lung tumors found in the radiography arm were at stage I. LDCT decreased all-cause mortality by 6.7% and lung cancer mortality by 20% seven years after the trial's start(60). There is currently no data on how cost-effective LDCT screening is in NLST(61).

Advances and Challenges in Lung Cancer Treatment

Lung cancer is among the most common diseases worldwide. Surgical excision is the main therapy for preliminary NSCLC (stage I/II), which is frequently followed by adjuvant therapy. Treatment usually switches to chemoradiotherapy for more advanced disease (stage III/IV). Conventional chemotherapeutic drugs have limitations that limit treatment efficacy, such as Drug resistance, inadequate absorption, and non-specific targeting(51).

By protecting therapeutic compounds from degradation and enabling tailored distribution to

tumor locations, nanodrug delivery devices can lower off-target toxicity and improve anticancer efficacy. Enhanced drug bioavailability, The benefits of nanocarrier-based administration include enhanced safety via site-specific delivery and the capacity for controlled and prolonged release.

Nanomedicine is a substitute for conventional chemotherapy that may reduce systemic side effects(62).

Molecular targeted therapy has become more important in the treatment of non-small cell lung cancer (NSCLC). Hepatocyte growth factor receptor (c-MET), epidermal growth factor receptor (EGFR), and anaplastic lymphoma kinase (ALK) are examples of receptor tyrosine kinases that are important targets for molecular treatments. Tyrosine kinase inhibitors (TKIs) targeting EGFR mutations include gefitinib and erlotinib. Inhibitors directed at other oncogenic drivers are also under investigation. Although targeted therapies show initial effectiveness, their long-term efficacy is limited by acquired resistance, which often develops due to tumor heterogeneity and epigenetic changes, emphasizing the need to identify novel molecular targets for therapy(63).

With positive tumor control outcomes, photothermal therapy is seen as a viable minimally invasive treatment option. In photothermal therapy, light energy is converted into heat to ablate tumors by combining photothermal agents with localized laser irradiation. The combination of photothermal therapy and nanotechnology shows promising results and synergistic anticancer effects(64).

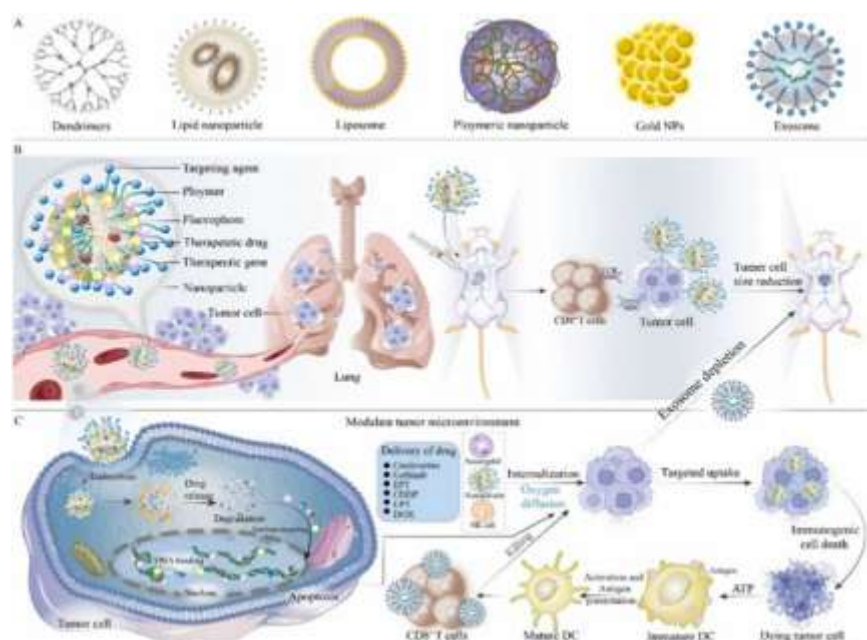
Immunotherapy techniques, particularly immune checkpoint inhibitors, have demonstrated safety and effectiveness and provide NSCLC patients with additional therapeutic alternatives.



Combining immunotherapy with other forms of treatment may sometimes lead to better results(65).

Lung cancer still faces significant therapeutic obstacles despite advancements in treatment, and new, efficient approaches are desperately needed. With the goal of offering fresh perspectives on treatment development, this review highlights recent advancements in lung cancer immunotherapy, photothermal therapy, molecular targeted therapy, and nanomedicine delivery(66).

The structure of nanoparticles provides features including regulated drug release, improved stability of anticancer medications, and simplicity of surface modification. By delivering nucleic acids and anticancer drugs to tumor tissues, nanoparticles can significantly lower systemic side effects and boost treatment efficacy. An extensive analysis of lung cancer treatment with nanodrug delivery devices is provided in this section. The focus is on delivery strategies using various nanoparticle types, including as exosomes, magnetic particles, and polymer-based particles. Included are lipid, liposomal nanoparticles, and poly(lactic co-glycolic acid) (PLGA) (62).



1. Exosomes — Line-by-Line Citations

Exosomes are bio-derived nanocarriers that range in size from 30 to 150 nm and have lipid bilayers. They are comparatively immunogenic, stable, and biocompatible. Exosomes are now a crucial nanocarrier platform for encasing nucleic acids and chemotherapeutic medicines, allowing for effective targeted drug delivery and greatly improving precision therapy in lung cancer (66). Exosome-associated AAV (AAVExo) significantly enhanced gene transfer efficiency in

both NSCLC and SCLC cells compared with conventional AAV. Paclitaxel has also been administered using exosomes made from cow's colostrum(PAC), and oral folic acid-decorated ExoPAC treatment showed markedly improved therapeutic efficacy and safety. Moreover, doxorubicin (DOX) and vorinostat have been delivered using artificial exosomes (AEs), which not only facilitate transport to tumor tissues but also prolong drug retention within tumors(67).

2. Polymeric Nanoparticles



Polymeric nanoparticles (PNPs) consist of both colloidal and solid micellar components and are classified into three forms: nanospheres, nanocapsules, and polymer micelles. As carriers for chemotherapeutic drugs, PNPs exhibit strong potential for cellular uptake and low cytotoxicity, allowing targeted delivery to lung cancer cells. Poly (ethylene glycol)-poly(ϵ -caprolactone) triblock copolymer nanoparticles (PEG-PCL-PEG, PECE), which are biodegradable, were used to co-deliver sorafenib and crizotinib, effectively inhibiting lung cancer progression in vivo(68). Lipid-polymer hybrid nanoparticles (NI/HA-DDP LPNs) and polymeric nanoparticles (NI/HA-DDP PNPs) loaded with cisplatin (DDP) and co-modified with nitroimidazole (NI) and HA were developed; NI/HA-DDP LPNs exhibited improved anticancer efficacy against drug-resistant A549/DDP lung cancer cells. Paclitaxel and cisplatin-loaded RGD-modified lipid polymer nanoparticles showed remarkable anticancer efficacy in vitro and in vivo. In a lung cancer xenograft model, amphiphilic copolymer nanoparticles co-delivering cisplatin and regorafenib consistently reduced lung cancer progression at acceptable levels(69).

3. Magnetic Nanoparticles

Because of their magnetic and superparamagnetic characteristics, magnetic nanoparticles (MNPs) are extensively used in biomedicine. The FDA has authorized iron oxide-based magnetic nanoparticles with good biocompatibility for use in clinical settings as magnetic resonance imaging (MRI) contrast agents and iron supplements. Because of their high tissue penetration ability, superparamagnetic iron oxide nanoparticles (SPIONs) are utilized as T2-weighted negative contrast agents in magnetic resonance imaging (MRI). It has been observed that a multifunctional drug-loaded nanoparticle system (F/A

PLGA@DOX/SPIO) increases lung cancer cells' production of reactive oxygen species (ROS). The erlotinib formulation VT-287, which contains magnetic nanoparticles, has shown cytotoxic effects against lung cancer cells in vitro and preferred lung-targeted drug delivery in vivo, demonstrating its safety and effectiveness in lung cancer therapy(70).

4. Lipid Nanoparticles (LNP)

Lipid nanoparticles (LNPs) are a successful medication delivery method that can overcome lung biological barriers. Preclinical research has shown that LNP siRNA formulations are highly effective in silencing genes. Encapsulation of microRNA-126 (miR-126-3p) mimic and microRNA-221 (miR-221-3p) inhibitor in LNPs significantly inhibited the growth of patient-derived lung cancer xenografts by suppressing the PI3K/AKT signaling pathway through PIK3R2/AKT downregulation. Additionally, adding ligands specific to tumor cells to the lipid surface of LNPs can decrease systemic toxicity while improving the therapeutic efficacy of miRNA delivery(71).

5. Poly(lactic-co-glycolic) Acid (PLGA) Nanoparticles

The FDA has approved poly(lactic-co-glycolic) acid (PLGA), a biocompatible and biodegradable polymer with a high drug-loading capacity, outstanding stability, and sustained and controlled drug release characteristics. Cisplatin and upconversion nanoparticles were co-delivered via RGD receptor-targeted PLGA nanoparticles, which demonstrated better cisplatin efficacy and tolerance in addition to increased cytotoxicity against lung cancer cells. Sorafenib was delivered to lung cancer cells using a chitosan-PLGA folic acid (FA) nanocarrier, which demonstrated

targeted transport and efficient tumor cell proliferation inhibition(72).

6. Liposomes

Liposomes are anticipated to increase the efficacy of lung cancer targeted therapy by acting as a medication delivery system. On A549 lung cancer cells, a liposome formulation co-loaded with curcumin and paclitaxel (PTX) modified via RGD demonstrated outstanding antiproliferative activities. In lung cancer xenograft mice, folic acid (FA)-modified liposomal nanoparticles designed to specifically co-deliver MT1DP and erastin demonstrated potent therapeutic benefits and enhanced bioavailability of the combination therapy. To enhance tumor targeting, co-delivery liposomes containing dioscin and RPV-modified epirubicin were developed, and they demonstrated strong anticancer effect in vivo(73) .

Radiotherapy for Lung Cancer

One crucial treatment option for lung cancer is radiation therapy. Although radiation therapy is currently underutilized in clinical practice, around Evidence-based treatment is prescribed for 77% of lung cancer patients. These advancements have improved clinical results, such as increased survival and decreased treatment-related toxicity, and broadened the indications for radiation in lung cancer. This study looks at how radiotherapy is currently used to treat lung cancer, talks about the data supporting its usage, and suggests future paths for radiotherapy treatment approaches(74).

Advances in Radiotherapy Technologies

Rapid advancements in radiation technology are enhancing treatment precision, speed, and safety. Imaging is a crucial component of radiation delivery precision. 4DCT, or four-dimensional computed tomography, enables the evaluation of

patient-specific tumor mobility and may be integrated into treatment plans to guarantee specified dose administration independent of tumor position, is now widely used in radiotherapy planning. Cone beam computed tomography (CBCT) in conjunction with linear accelerators enables tumor position verification both before and during treatment(75).

Stereotactic ablative body radiation (SABR) administration has been made possible by the development of sophisticated imaging technology and better patient immobilization techniques. SABR provides excellent geometric precision and accuracy while delivering substantial ablative doses in fewer fractions.(76).The enormous margins that were previously required for conventional radiation in order to account for tumor movements and setup uncertainty have been reduced thanks to improved imaging. As a result, the unintentional dose to nearby healthy tissues and the resulting harm have decreased. Intensity modulated radiation therapy (IMRT) reduces exposure to healthy tissue and improves dose distribution conformality by applying multiple beams of different intensities to the tumor(77).

An alternative technique called respiratory gating only activates the radiation beam when the tumor is at a particular position, taking tumor movements into account. Breath-hold techniques, where the patient temporarily pauses breathing at a specific phase of the respiratory cycle during gradual treatment delivery, can be used to achieve respiratory gating. However, breath hold gating may be challenging for those with underlying lung conditions. Another gating technique is to monitor the tumor's growth and only turn on the laser when it reaches a specific location. This approach may sometimes require the use of specialized tracking systems or implanted fiducial markers. These advances have made modern radiation therapy



increasingly important in improving the prognosis of lung cancer patients across all stages(78).

Radiotherapy for Stage I and II NSCLC

Stereotactic ablative body radiation (SABR) is currently used for patients with peripherally localized stage I–IIA non-small cell lung cancer (NSCLC) who are either medically inoperable or decline surgery. Two randomized controlled trials comparing SABR with conventional radiotherapy have confirmed its effectiveness in early-stage NSCLC treatment. Most participants in both studies were over the median age of 70 years and had significant comorbid conditions (79). In patients treated with SABR who showed similar toxicity profiles and quality of life, the CHISEL study was the first to report improved overall survival (OS) (2-year OS: 77% vs. 59%, $P = 0.027$). A lower rate of pathological confirmation, the use of 4DCT and PET staging in the SPACE trial, and varying radiation doses in the conventional arms could all contribute to variations in survival results between studies(80).

Radiotherapy for Stage III NSCLC

A lower rate of pathological confirmation, the use of 4DCT and PET staging in the SPACE trial, and varying radiation doses in the conventional arms could all contribute to variations in survival results between studies(81).

Intensity modulated radiation treatment (IMRT) was administered to 47% of patients; these patients had considerably bigger tumor volumes and higher disease stages. IMRT use was linked to lower frequencies of grade 3 radiation pneumonitis and lower cardiac radiation doses in secondary study. The use of IMRT did not significantly affect survival. However, higher heart radiation doses had a negative impact on survival on multivariate analysis, suggesting that strategies to reduce

cardiac exposure would be beneficial over time(82).

Radiotherapy for Stage IV NSCLC

Non-small cell lung cancer (NSCLC) in stage IV is typically regarded as incurable. However, ablative treatment of all metastatic locations may lead to long-term survival in certain individuals with oligometastatic illness. A European agreement now defines synchronous oligometastases as up to five distant metastases involving no more than three organs, detected utilizing comprehensive imaging such as brain MRI and PET. Until recently, there was no widely recognized definition of oligometastases(83).

Two trials specifically aimed at NSCLC were ended early due to notable improvements observed in the ablative therapy group. Only patients who had first-line systemic medication and showed no signs of illness progression were eligible for both studies(84). These studies showed that ablative therapy significantly improved progression-free survival (PFS), despite higher toxicity and no treatment-related mortality. All patients received standard systemic therapy in a pooled analysis by Sarit B. Palma et al. that encompassed several primary tumor types, including around 18% NSCLC; a significant PFS benefit was noted, despite a 5% treatment-related death rate(85).

FUTURE DIRECTIONS

Radiotherapy and Immunotherapy

Combining immunotherapy with radiation is an exciting field of current study. By altering the tumor microenvironment, releasing cytokines and chemokines, encouraging leukocyte infiltration, and making tumor cells more vulnerable to immunogenic cell death, radiotherapy affects the immune system in a number of ways. Ionizing



radiation can act as an in situ personalized vaccine in some patients, enhancing immunogenicity and improving the effects of immunotherapy by amplifying danger signals(86). Recent evidence from clinical trials supports these preclinical findings, showing that patients who underwent radiotherapy before immunotherapy had better overall survival (OS). This implies that radiation therapy and immune checkpoint inhibitor therapy may interact favorably and even synergistically(87).

New Radiotherapy Technologies

Significant improvements in radiation technologies during the last 20 years have improved survival rates, reduced toxicities, and expanded treatment eligibility. One of the The MRI linac, which enables tumor viewing during therapy and real-time adaptation Reacting to changes in tumor or normal tissues is one possible new approach(88).

In SABR, real-time adaptive MRI-based radiation has been evaluated for ultracentral and peripheral cancers. MRI-guided adaptive therapy improves the therapeutic ratio for central malignancies by ensuring adequate tumor dose coverage while respecting dosage limitations on adjacent mediastinal tissues. however there is limited clinical benefit for peripheral tumors. This may reduce the significant toxicities linked to conventional linear accelerator-based SABR for central cancers(89).

Machine Learning and Big Data

Clinical and imaging data are abundant in the field of radiotherapy, and a large portion of this data is available for analysis and kept in electronic oncology information systems. Predicting treatment results, assigning risk groups, and assisting clinician-patient decision-making are all

possible with machine learning that integrates clinical and imaging characteristics (radiomics). Distributed learning networks spanning several centers can enable model training without data leaving any one institution, hence addressing privacy concerns (90). Continuous quick learning with outcomes integrated into point-of-care decision support systems is the aim. Although it hasn't been extensively tested in clinical practice yet, this method promises to personalize radiation decisions beyond strict clinical trial requirements (90).

Palliative and Supportive Care of Lung Cancer

Patients with lung cancer often face numerous long-term physical and psychological issues in addition to a dismal prognosis. These symptoms can lower quality of life, cause significant difficulties, and hinder social and physical functioning. The evidence-based therapies that provide the best Palliative and supportive care for lung patients cancer are reviewed in this section. To demonstrate the growing body of data, treatments for dyspnea, one of the most prevalent symptoms this population experiences, are examined(91).

When it comes to the pharmacological treatment of dyspnea, systemic opioids offer the best evidence. In particular, there is strong evidence supporting systemic morphine, which is best administered as a once-daily sustained release medication. Additionally, there is mounting evidence supporting a number of non-pharmacological supplemental therapy for the management of dyspnea. Interventions that have been demonstrated to improve Pursed lip breathing, diaphragmatic breathing, posture, and pacing tactics are all examples of effective breathing().



More study is required, although psychosocial therapy targeted at easing discomfort and anxiety may help improve dyspnea management. Case management strategies and nurse-led follow-up programs have been shown to effectively reduce psychological distress and dyspnea. These models provide useful frameworks for implementing evidence-based strategies for managing symptoms(104).

Lung Cancer Symptom Burden and Supportive Care Needs

An estimated 43% of lung cancer patients experience psychological distress, compared with an overall rate of 35% across 14 cancer types. Reduced social and physical functioning, along with substantial disease burden, contribute to a poorer quality of life. Patients newly diagnosed with lung cancer often report feelings of shock and fear, as well as a high need for information. Because lung cancer is so severe, research has revealed that individuals with this disease report higher levels of psychological pain and unmet daily life demands than patients with other diseases(10). This study evaluates evidence-based interventions aimed at improving best-practice supportive and palliative care for individuals with lung cancer. To demonstrate the growing body of evidence, pharmacological and nonpharmacological treatments for dyspnea—one of the most prevalent symptoms in this group—are examined. Additionally reviewed is the evidence in favor of interventions that target psychological distress and unmet needs. Additionally, we take into account current research on health service-level treatments intended to attain the best results in this population, given the complicated health and support requirements of lung cancer patients(91).

Recent Developments and New Methods of Lung Cancer Diagnosis

Cancer, one of the worst diseases, is characterized by rapid, abnormal, and unregulated cell division that can spread to other organs. This review focuses on analyzing current and emerging diagnostic techniques for the detection of lung cancer. Lung cancer remains a leading cause of mortality, particularly among smokers, and its incidence is increasing in nonsmokers due to factors such as exposure to secondhand smoke. Environmental factors and lifestyle modifications are linked to high lung cancer mortality(10).

While tuberculosis is less common in Western nations like the United States, the United Kingdom, and Canada, lung cancer is frequently misdiagnosed as TB in India due to the high prevalence of TB. The fact that symptoms usually appear late after considerable tumor dissemination presents a significant management problem for lung cancer. For early detection, precise staging, and treatment planning, this calls for extremely sophisticated diagnostic methods. Novel biomarkers and biosensors for molecular detection, radiogenomics connecting imaging phenotypes with genetic profiles, and artificial intelligence-based diagnostic algorithms are examples of current and developing techniques.(93). These cutting-edge approaches expand upon traditional methods that have been developed throughout time for increased sensitivity and diagnostic accuracy, such as bronchoscopy, sputum cytology, CT imaging, and biopsy. Additionally, the review sheds light on regulatory frameworks including IDE and CLIA certification for diagnostic equipment used in Australia, Japan, India, and the United States(94).

Multidisciplinary Team in Lung Cancer

In the treatment of lung cancer, multidisciplinary care (MDC) is regarded as best practice. By establishing multidisciplinary team (MDT) meetings, health care providers have invested



heavily in MDC. As lung cancer treatment develops and includes new treatments and diagnostic advancements, this spending is probably going to continue. MDT meetings must be successful, efficient, and flexible enough to promote best practices and introduce new ideas. The "evidence–practice gaps" in the application of lung cancer MDC are examined in this article. These gaps result from recurring issues found in previous research and systematic reviews. We examine how implementation science and quality improvement frameworks can help close these gaps by strengthening the adoption of innovations by MDTs and better translating findings into practice(95).

Global Advance and future direction in lung cancer

Over the past ten years, lung cancer care has significantly improved due to advancements in early detection, therapy, and prevention. These days, non-tobacco risk factor identification, screening program implementation, and incidental nodule monitoring are all part of prevention measures that go beyond tobacco control. Despite decreases in smoking incidence and growing efforts to lower particulate matter exposure, primary prevention progress is still inconsistent, with notable regional differences(96).

Lung cancer remains the leading cause of cancer-related mortality worldwide. The 3-year relative survival rate for non-small-cell lung cancer (NSCLC) increased from 26% in 2004 to 43% in 2018, while that for small-cell lung cancer (SCLC) rose from 9% to 12%. Despite significant advancements in treatment, early detection, and prevention, treatment resistance and unequal access continue to impede the best outcomes. A multidisciplinary council was established by the New York Lung Cancer Foundation (NYLCF) to address these issues and establish priorities for

research and care. This article condenses the NYLCF 2025 Summit discussions into actionable, stage-specific tasks and system-level suggestions(97).

CONCLUSION

lung cancer is still one of the top causes of cancer-related deaths in the world. While advances in molecular profiling, personalized therapy, and early detection have started to improve patient outcomes. New opportunities for individualized care are provided by developments in immunotherapy, nanomedicine, and AI-driven diagnostics. Persistent challenges, including therapeutic resistance, late diagnosis, and disparities in access, highlight the need for multidisciplinary, equitable, and technology-integrated strategies. Ongoing research and collaboration are essential to translate these advances into real-world survival benefits for all patients.

REFERENCES

1. Hanahan D, Weinberg RA. Hallmarks of Cancer: The Next Generation. *Cell*. 2011 Mar;144(5):646–74. doi:10.1016/j.cell.2011.02.013
2. De Leyn P, Doooms C, Kuzdzal J, Lardinois D, Passlick B, Rami-Porta R, et al. Revised ESTS guidelines for preoperative mediastinal lymph node staging for non-small-cell lung cancer. *European Journal of Cardio-Thoracic Surgery*. 2014 May 1;45(5):787–98. doi:10.1093/ejcts/ezu028
3. Weinberg RA. *The biology of cancer*. Second edition. New York, NY: Garland Science; 2014. 1 p. doi:10.1201/9780429258794
4. Travis WD, Brambilla E, Nicholson AG, Yatabe Y, Austin JHM, Beasley MB, et al. The 2015 World Health Organization Classification of Lung Tumors. *Journal of*



- Thoracic Oncology. 2015 Sep;10(9):1243–60. doi:10.1097/JTO.0000000000000630
5. Herbst RS, Heymach JV, Lippman SM. Lung Cancer. *N Engl J Med.* 2008 Sep 25;359(13):1367–80. doi:10.1056/NEJMra0802714
 6. Park IW, Wistuba II, Maitra A, Milchgrub S, Virmani AK, Minna JD, et al. Multiple Clonal Abnormalities in the Bronchial Epithelium of Patients With Lung Cancer. *JNCI Journal of the National Cancer Institute.* 1999 Nov 3;91(21):1863–8. doi:10.1093/jnci/91.21.1863
 7. Salgia R, Skarin AT. Molecular abnormalities in lung cancer. *JCO.* 1998 Mar;16(3):1207–17. doi:10.1200/JCO.1998.16.3.1207
 8. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA A Cancer J Clinicians.* 2021 May;71(3):209–49. doi:10.3322/caac.21660
 9. Bade BC, Dela Cruz CS. Lung Cancer 2020. *Clinics in Chest Medicine.* 2020 Mar;41(1):1–24. doi:10.1016/j.ccm.2019.10.001
 10. Ferlay J, Colombet M, Soerjomataram I, Mathers C, Parkin DM, Piñeros M, et al. Estimating the global cancer incidence and mortality in 2018: GLOBOCAN sources and methods. *Intl Journal of Cancer.* 2019 Apr 15;144(8):1941–53. doi:10.1002/ijc.31937
 11. Mathur P, Sathishkumar K, Chaturvedi M, Das P, Sudarshan KL, Santhappan S, et al. Cancer Statistics, 2020: Report From National Cancer Registry Programme, India. *JCO Global Oncology.* 2020 Nov;(6):1063–75. doi:10.1200/GO.20.00122
 12. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA A Cancer J Clinicians.* 2018 Nov;68(6):394–424. doi:10.3322/caac.21492
 13. Rosell R, Moran T, Queralt C, Porta R, Cardenal F, Camps C, et al. Screening for Epidermal Growth Factor Receptor Mutations in Lung Cancer. *N Engl J Med.* 2009 Sep 3;361(10):958–67. doi:10.1056/NEJMoa0904554
 14. Rosell R, Moran T, Queralt C, Porta R, Cardenal F, Camps C, et al. Screening for Epidermal Growth Factor Receptor Mutations in Lung Cancer. *N Engl J Med.* 2009 Sep 3;361(10):958–67. doi:10.1056/NEJMoa0904554
 15. Herbst RS, Morgensztern D, Boshoff C. The biology and management of non-small cell lung cancer. *Nature.* 2018 Jan;553(7689):446–54. doi:10.1038/nature25183
 16. Herbst RS, Heymach JV, Lippman SM. Lung Cancer. *N Engl J Med.* 2008 Sep 25;359(13):1367–80. doi:10.1056/NEJMra0802714
 17. Mok TS, Wu YL, Thongprasert S, Yang CH, Chu DT, Saijo N, et al. Gefitinib or Carboplatin–Paclitaxel in Pulmonary Adenocarcinoma. *N Engl J Med.* 2009 Sep 3;361(10):947–57. doi:10.1056/NEJMoa0810699
 18. Pao W, Girard N. New driver mutations in non-small-cell lung cancer. *The Lancet Oncology.* 2011 Feb;12(2):175–80. doi:10.1016/S1470-2045(10)70087-5
 19. Gerlinger M, Rowan AJ, Horswell S, Larkin J, Endesfelder D, Gronroos E, et al. Intratumor Heterogeneity and Branched Evolution Revealed by Multiregion Sequencing. *N Engl J Med.* 2012 Mar 8;366(10):883–92. doi:10.1056/NEJMoa1113205
 20. Swanton C. Intratumor Heterogeneity: Evolution through Space and Time. *Cancer*

- Research. 2012 Oct 1;72(19):4875–82. doi:10.1158/0008-5472.CAN-12-2217
21. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA A Cancer J Clinicians*. 2018 Nov;68(6):394–424. doi:10.3322/caac.21492
22. Survival of Patients with Stage I Lung Cancer Detected on CT Screening. *N Engl J Med*. 2006 Oct 26;355(17):1763–71. doi:10.1056/NEJMoa060476
23. Hecht SS. Tobacco Smoke Carcinogens and Lung Cancer. *JNCI Journal of the National Cancer Institute*. 1999 Jul 21;91(14):1194–210. doi:10.1093/jnci/91.14.1194
24. Stratton MR, Campbell PJ, Futreal PA. The cancer genome. *Nature*. 2009 Apr;458(7239):719–24. doi:10.1038/nature07943
25. Vogelstein B, Papadopoulos N, Velculescu VE, Zhou S, Diaz LA, Kinzler KW. Cancer Genome Landscapes. *Science*. 2013 Mar 29;339(6127):1546–58. doi:10.1126/science.1235122
26. Mardis ER. Next-Generation Sequencing Platforms. *Annual Rev Anal Chem*. 2013 Jun 12;6(1):287–303. doi:10.1146/annurev-anchem-062012-092628
27. Kim CFB, Jackson EL, Woolfenden AE, Lawrence S, Babar I, Vogel S, et al. Identification of Bronchioalveolar Stem Cells in Normal Lung and Lung Cancer. *Cell*. 2005 Jun;121(6):823–35. doi:10.1016/j.cell.2005.03.032
28. Beer DG, Kardia SLR, Huang CC, Giordano TJ, Levin AM, Misek DE, et al. Gene-expression profiles predict survival of patients with lung adenocarcinoma. *Nat Med*. 2002 Aug;8(8):816–24. doi:10.1038/nm733
29. Pao W, Girard N. New driver mutations in non-small-cell lung cancer. *The Lancet Oncology*. 2011 Feb;12(2):175–80. doi:10.1016/S1470-2045(10)70087-5
30. Shaw AT, Yeap BY, Mino-Kenudson M, Digumarthy SR, Costa DB, Heist RS, et al. Clinical Features and Outcome of Patients With Non–Small-Cell Lung Cancer Who Harbor EML4-ALK. *JCO*. 2009 Sep 10;27(26):4247–53. doi:10.1200/JCO.2009.22.6993
31. Shaw AT, Yeap BY, Mino-Kenudson M, Digumarthy SR, Costa DB, Heist RS, et al. Clinical Features and Outcome of Patients With Non–Small-Cell Lung Cancer Who Harbor EML4-ALK. *JCO*. 2009 Sep 10;27(26):4247–53. doi:10.1200/JCO.2009.22.6993
32. Bass AJ, Watanabe H, Mermel CH, Yu S, Perner S, Verhaak RG, et al. SOX2 is an amplified lineage-survival oncogene in lung and esophageal squamous cell carcinomas. *Nat Genet*. 2009 Nov;41(11):1238–42. doi:10.1038/ng.465
33. Weiss J, Sos ML, Seidel D, Peifer M, Zander T, Heuckmann JM, et al. Frequent and Focal FGFR1 Amplification Associates with Therapeutically Tractable FGFR1 Dependency in Squamous Cell Lung Cancer. *Sci Transl Med*. 2010 Dec 15;2(62). doi:10.1126/scitranslmed.3001451
34. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA A Cancer J Clinicians*. 2018 Nov;68(6):394–424. doi:10.3322/caac.21492
35. Travis WD, Brambilla E, Nicholson AG, Yatabe Y, Austin JHM, Beasley MB, et al. The 2015 World Health Organization Classification of Lung Tumors. *Journal of Thoracic Oncology*. 2015 Sep;10(9):1243–60. doi:10.1097/JTO.0000000000000630

36. Herbst RS, Heymach JV, Lippman SM. Lung Cancer. *N Engl J Med.* 2008 Sep 25;359(13):1367–80. doi:10.1056/NEJMra0802714
37. Rivera MP, Mehta AC, Wahidi MM. Establishing the Diagnosis of Lung Cancer. *Chest.* 2013 May;143(5):e142S-e165S. doi:10.1378/chest.12-2353
38. Turajlic S, Swanton C. Metastasis as an evolutionary process. *Science.* 2016 Apr 8;352(6282):169–75. doi:10.1126/science.aaf2784
39. Soria JC, Mok TS, Cappuzzo F, Jänne PA. EGFR-mutated oncogene-addicted non-small cell lung cancer: Current trends and future prospects. *Cancer Treatment Reviews.* 2012 Aug;38(5):416–30. doi:10.1016/j.ctrv.2011.10.003
40. Nicholson AG, Tsao MS, Beasley MB, Borczuk AC, Brambilla E, Cooper WA, et al. The 2021 WHO Classification of Lung Tumors: Impact of Advances Since 2015. *Journal of Thoracic Oncology.* 2022 Mar;17(3):362–87. doi:10.1016/j.jtho.2021.11.003
41. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA A Cancer J Clinicians.* 2021 May;71(3):209–49. doi:10.3322/caac.21660
42. Travis WD, Brambilla E, Noguchi M, Nicholson AG, Geisinger K, Yatabe Y, et al. Diagnosis of Lung Cancer in Small Biopsies and Cytology: Implications of the 2011 International Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society Classification. *Archives of Pathology and Laboratory Medicine.* 2013 May;137(5):668–84. doi:10.5858/arpa.2012-0263-RA
43. Travis WD, Brambilla E, Nicholson AG, Yatabe Y, Austin JHM, Beasley MB, et al. The 2015 World Health Organization Classification of Lung Tumors. *Journal of Thoracic Oncology.* 2015 Sep;10(9):1243–60. doi:10.1097/JTO.0000000000000630
44. Vilmann P, Clementsen P, Colella S, Siemsen M, De Leyn P, Dumonceau JM, et al. Combined endobronchial and esophageal endosonography for the diagnosis and staging of lung cancer: European Society of Gastrointestinal Endoscopy (ESGE) Guideline, in cooperation with the European Respiratory Society (ERS) and the European Society of Thoracic Surgeons (ESTS). *Endoscopy.* 2015 Jun 1;47(06):545–59. doi:10.1055/s-0034-1392040
45. Shiratsuchi H, Wang Z, Chen G, Ray P, Lin J, Zhang Z, et al. Oncogenic Potential of CYP24A1 in Lung Adenocarcinoma. *Journal of Thoracic Oncology.* 2017 Feb;12(2):269–80. doi:10.1016/j.jtho.2016.10.010
46. Ost DE, Niu J, Elting LS, Buchholz TA, Giordano SH. Quality Gaps and Comparative Effectiveness in Lung Cancer Staging and Diagnosis. *Chest.* 2014 Feb;145(2):331–45. doi:10.1378/chest.13-1599
47. Rivera MP, Mehta AC, Wahidi MM. Establishing the Diagnosis of Lung Cancer. *Chest.* 2013 May;143(5):e142S-e165S. doi:10.1378/chest.12-2353
48. Rivera MP, Mehta AC, Wahidi MM. Establishing the Diagnosis of Lung Cancer. *Chest.* 2013 May;143(5):e142S-e165S. doi:10.1378/chest.12-2353
49. Rivera MP, Mehta AC, Wahidi MM. Establishing the Diagnosis of Lung Cancer. *Chest.* 2013 May;143(5):e142S-e165S. doi:10.1378/chest.12-2353
50. Rivera MP, Mehta AC, Wahidi MM. Establishing the Diagnosis of Lung Cancer.

- Chest. 2013 May;143(5):e142S-e165S. doi:10.1378/chest.12-2353
51. Rivera MP, Mehta AC, Wahidi MM. Establishing the Diagnosis of Lung Cancer. *Chest*. 2013 May;143(5):e142S-e165S. doi:10.1378/chest.12-2353
52. Rivera MP, Mehta AC, Wahidi MM. Establishing the Diagnosis of Lung Cancer. *Chest*. 2013 May;143(5):e142S-e165S. doi:10.1378/chest.12-2353
53. Rivera MP, Mehta AC, Wahidi MM. Establishing the Diagnosis of Lung Cancer. *Chest*. 2013 May;143(5):e142S-e165S. doi:10.1378/chest.12-2353
54. Rivera MP, Mehta AC, Wahidi MM. Establishing the Diagnosis of Lung Cancer. *Chest*. 2013 May;143(5):e142S-e165S. doi:10.1378/chest.12-2353
55. Saab MM, McCarthy M, O'Driscoll M, Sahn LJ, Leahy-Warren P, Noonan B, et al. A systematic review of interventions to recognise, refer and diagnose patients with lung cancer symptoms. *npj Prim Care Respir Med*. 2022 Oct 18;32(1):42. doi:10.1038/s41533-022-00312-9
56. Larke FJ, Kruger RL, Cagnon CH, Flynn MJ, McNitt-Gray MM, Wu X, et al. Estimated Radiation Dose Associated With Low-Dose Chest CT of Average-Size Participants in the National Lung Screening Trial. *American Journal of Roentgenology*. 2011 Nov;197(5):1165-9. doi:10.2214/AJR.11.6533
57. Survival of Patients with Stage I Lung Cancer Detected on CT Screening. *N Engl J Med*. 2006 Oct 26;355(17):1763-71. doi:10.1056/NEJMoa060476
58. The National Lung Screening Trial Research Team. Reduced Lung-Cancer Mortality with Low-Dose Computed Tomographic Screening. *N Engl J Med*. 2011 Aug 4;365(5):395-409. doi:10.1056/NEJMoa1102873
59. The National Lung Screening Trial Research Team. Reduced Lung-Cancer Mortality with Low-Dose Computed Tomographic Screening. *N Engl J Med*. 2011 Aug 4;365(5):395-409. doi:10.1056/NEJMoa1102873
60. The National Lung Screening Trial Research Team. Reduced Lung-Cancer Mortality with Low-Dose Computed Tomographic Screening. *N Engl J Med*. 2011 Aug 4;365(5):395-409. doi:10.1056/NEJMoa1102873
61. Wisnivesky JP, Mushlin AI, Sicherman N, Henschke C. The Cost-Effectiveness of Low-Dose CT Screening for Lung Cancer*. *Chest*. 2003 Aug;124(2):614-21. doi:10.1378/chest.124.2.614
62. Soria JC, Ohe Y, Vansteenkiste J, Reungwetwattana T, Chewaskulyong B, Lee KH, et al. Osimertinib in Untreated EGFR - Mutated Advanced Non-Small-Cell Lung Cancer. *N Engl J Med*. 2018 Jan 11;378(2):113-25. doi:10.1056/NEJMoa1713137
63. Morvan MG, Lanier LL. NK cells and cancer: you can teach innate cells new tricks. *Nat Rev Cancer*. 2016 Jan;16(1):7-19. doi:10.1038/nrc.2015.5
64. Kim D, Kim H. Optimization of Photothermal Therapy Treatment Effect under Various Laser Irradiation Conditions. *IJMS*. 2022 May 25;23(11):5928. doi:10.3390/ijms23115928
65. Peng T, Wu T. Efficacy of PD-1/PD-L1 inhibitors in patients with advanced non-small cell lung cancer: A meta-analysis of randomized clinical trials. *Thoracic Cancer*. 2019 May;10(5):1176-81. doi:10.1111/1759-7714.13060
66. Kim D, Kim H. Optimization of Photothermal Therapy Treatment Effect under Various

- Laser Irradiation Conditions. *IJMS*. 2022 May 25;23(11):5928. doi:10.3390/ijms23115928
67. Li H, Li S, Lin Y, Chen S, Yang L, Huang X, et al. Artificial exosomes mediated spatiotemporal-resolved and targeted delivery of epigenetic inhibitors. *J Nanobiotechnol*. 2021 Nov 17;19(1):364. doi:10.1186/s12951-021-01107-9
68. Patra JK, Das G, Fraceto LF, Campos EVR, Rodriguez-Torres MDP, Acosta-Torres LS, et al. Nano based drug delivery systems: recent developments and future prospects. *J Nanobiotechnol*. 2018 Dec;16(1):71. doi:10.1186/s12951-018-0392-8
69. Wang S, Gou J, Wang Y, Tan X, Zhao L, Jin X, et al. Synergistic Antitumor Efficacy Mediated by Liposomal Co-Delivery of Polymeric Micelles of Vinorelbine and Cisplatin in Non-Small Cell Lung Cancer. *IJN*. 2021 Mar;Volume 16:2357–72. doi:10.2147/IJN.S290263
70. Pankhurst QA, Connolly J, Jones SK, Dobson J. Applications of magnetic nanoparticles in biomedicine. *J Phys D: Appl Phys*. 2003 Jul 7;36(13):R167–81. doi:10.1088/0022-3727/36/13/201
71. Hou X, Zaks T, Langer R, Dong Y. Lipid nanoparticles for mRNA delivery. *Nat Rev Mater*. 2021 Aug 10;6(12):1078–94. doi:10.1038/s41578-021-00358-0
72. Kakavandi S, Zare I, Esmailnejad N, Sarhadi M, Hheidari A, Shojaei S, et al. PLGA-integrated micro/nanoparticles for cargo delivery and nanomedicine of lung cancer. *International Journal of Pharmaceutics*. 2026 Jan;687:126339. doi:10.1016/j.ijpharm.2025.126339
73. Gai C, Liu C, Wu X, Yu M, Zheng J, Zhang W, et al. MT1DP loaded by folate-modified liposomes sensitizes erastin-induced ferroptosis via regulating miR-365a-3p/NRF2 axis in non-small cell lung cancer cells. *Cell Death Dis*. 2020 Sep 14;11(9):751. doi:10.1038/s41419-020-02939-3
74. Pardo-Sánchez JM, Mancheño N, Cerón J, Jordá C, Ansotegui E, Juan Ó, et al. Increased Tumor Growth Rate and Mesenchymal Properties of NSCLC-Patient-Derived Xenograft Models during Serial Transplantation. *Cancers*. 2021 Jun 14;13(12):2980. doi:10.3390/cancers13122980
75. Pardo-Sánchez JM, Mancheño N, Cerón J, Jordá C, Ansotegui E, Juan Ó, et al. Increased Tumor Growth Rate and Mesenchymal Properties of NSCLC-Patient-Derived Xenograft Models during Serial Transplantation. *Cancers*. 2021 Jun 14;13(12):2980. doi:10.3390/cancers13122980
76. Iyengar P, All S, Berry MF, Boike TP, Bradfield L, Dingemans AMC, et al. Treatment of Oligometastatic Non-Small Cell Lung Cancer: An ASTRO/ESTRO Clinical Practice Guideline. *Practical Radiation Oncology*. 2023 Sep;13(5):393–412. doi:10.1016/j.prro.2023.04.004
77. Xu C, Wu J, Liu B, Meng H, Zhao L, Wang P, et al. Simultaneous integrated dose reduction intensity-modulated radiotherapy improves survival in patients with locally advanced non-small cell lung cancer by reducing cardiac irradiation exposure. *Discov Onc*. 2025 Mar 12;16(1):300. doi:10.1007/s12672-025-02046-9
78. Shao K, Chen W, Xu Y, Yang S. Application of respiratory motion management technology for patients with lung cancer treated with stereotactic body radiotherapy (Review). *Oncol Lett*. 2025 Jun 27;30(3):1–12. doi:10.3892/ol.2025.15161
79. Tee ZH, Tsoi EHC, Lee Q, Wong YS, Gibson A, Parsons N, et al. Intrathecal Morphine and Post-Operative Pain Relief in Robotic

- Surgeries: A Systematic Review and Meta-Analysis. *JCM*. 2023 Dec 26;13(1):137. doi:10.3390/jcm13010137
80. Byrne A, De Abreu Lourenco R, Govindaraj R, Ball D, Le H. A cost-effectiveness analysis of stereotactic ablative radiotherapy versus conventionally fractionated radiotherapy in the management of stage 1 non-small-cell lung cancer: Results from the TROG 09.02 CHISEL study. *J Med Imag Rad Onc*. 2024 Oct;68(7):843–50. doi:10.1111/1754-9485.13755
81. Spigel DR, Faivre-Finn C, Gray JE, Vicente D, Planchard D, Paz-Ares L, et al. Five-Year Survival Outcomes From the PACIFIC Trial: Durvalumab After Chemoradiotherapy in Stage III Non–Small-Cell Lung Cancer. *JCO*. 2022 Apr 20;40(12):1301–11. doi:10.1200/JCO.21.01308
82. Bradley JD, Hu C, Komaki RR, Masters GA, Blumenschein GR, Schild SE, et al. Long-Term Results of NRG Oncology RTOG 0617: Standard- Versus High-Dose Chemoradiotherapy With or Without Cetuximab for Unresectable Stage III Non–Small-Cell Lung Cancer. *JCO*. 2020 Mar 1;38(7):706–14. doi:10.1200/JCO.19.01162
83. Iyengar P, All S, Berry MF, Boike TP, Bradfield L, Dingemans AMC, et al. Treatment of Oligometastatic Non-Small Cell Lung Cancer: An ASTRO/ESTRO Clinical Practice Guideline. *Practical Radiation Oncology*. 2023 Sep;13(5):393–412. doi:10.1016/j.prro.2023.04.004
84. Iyengar P, All S, Berry MF, Boike TP, Bradfield L, Dingemans AMC, et al. Treatment of Oligometastatic Non-Small Cell Lung Cancer: An ASTRO/ESTRO Clinical Practice Guideline. *Practical Radiation Oncology*. 2023 Sep;13(5):393–412. doi:10.1016/j.prro.2023.04.004
85. Iyengar P, All S, Berry MF, Boike TP, Bradfield L, Dingemans AMC, et al. Treatment of Oligometastatic Non-Small Cell Lung Cancer: An ASTRO/ESTRO Clinical Practice Guideline. *Practical Radiation Oncology*. 2023 Sep;13(5):393–412. doi:10.1016/j.prro.2023.04.004
86. Jung H, Paust S. Chemokines in the tumor microenvironment: implications for lung cancer and immunotherapy. *Front Immunol*. 2024 Jul 16;15:1443366. doi:10.3389/fimmu.2024.1443366
87. Wang X, Jing J. Cancer Immunotherapy in Combination with Radiotherapy and/or Chemotherapy: Mechanisms and Clinical Therapy. *MedComm*. 2025 Sep;6(9):e70346. doi:10.1002/mco2.70346
88. Kirkpatrick JP, Laack NN, Halasz LM, Minniti G, Chan MD. Proton Therapy for Brain Metastases: A Question of Value. *International Journal of Radiation Oncology*Biography*Physics*. 2018 Jul;101(4):830–2. doi:10.1016/j.ijrobp.2018.05.005
89. Kirkpatrick JP, Laack NN, Halasz LM, Minniti G, Chan MD. Proton Therapy for Brain Metastases: A Question of Value. *International Journal of Radiation Oncology*Biography*Physics*. 2018 Jul;101(4):830–2. doi:10.1016/j.ijrobp.2018.05.005
90. Crea F. Controversies in cardiac surgery: left main coronary disease, arterial myocardial revascularization, and prosthetic valves in dialysis. *European Heart Journal*. 2022 Nov 21;43(44):4603–5. doi:10.1093/eurheartj/ehac664
91. Feliciano JL, Waldfoegel JM, Sharma R, Zhang A, Gupta A, Sedhom R, et al. Pharmacologic Interventions for Breathlessness in Patients With Advanced Cancer: A Systematic Review and Meta-

- analysis. *JAMA Netw Open*. 2021 Feb 25;4(2):e2037632.
doi:10.1001/jamanetworkopen.2020.37632
92. Feliciano JL, Waldfoegel JM, Sharma R, Zhang A, Gupta A, Sedhom R, et al. Pharmacologic Interventions for Breathlessness in Patients With Advanced Cancer: A Systematic Review and Meta-analysis. *JAMA Netw Open*. 2021 Feb 25;4(2):e2037632.
doi:10.1001/jamanetworkopen.2020.37632
93. Nxumalo ZZ, Irusen EM, Allwood BW, Tadepalli M, Bassi J, Koegelenberg CFN. The utility of artificial intelligence in identifying radiological evidence of lung cancer and pulmonary tuberculosis in a high-burden tuberculosis setting. *S Afr Med J*. 2024 May 31;e1846.
doi:10.7196/SAMJ.2024.v114i6.1846
94. Ramesh M, Sah H, C. A. Regulatory Framework for In Vitro Diagnostic Devices in India: Current Landscape, Challenges, and Future Perspectives. *The Journal of Applied Laboratory Medicine*. 2026 Jan 5;11(1):125–42. doi:10.1093/jalm/jfaf164
95. Abelman R, Spring LM, Corcoran RB, Bardia A. Corrigendum to “Moving towards tissue-agnostic antibody drug conjugates: HER2 expression as the poster child.” *Annals of Oncology*. 2024 May;35(5):481. doi:10.1016/j.annonc.2023.12.004
96. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA A Cancer J Clinicians*. 2021 May;71(3):209–49. doi:10.3322/caac.21660
97. Meyer ML, Peters S, Jänne PA, Mok TS, Bunn PA, Abdel Karim N, et al. Global advances and future directions in lung cancer care: expert consensus and strategic priorities. *ESMO Open*. 2026 Feb;11(2):106034. doi:10.1016/j.esmoop.2025.106034

HOW TO CITE: Ashok Bendgude, Shubham Patil, Siddhi Shirahatti, Disha Fartade, Ajit Patil, Anilkumar Shinde, *Advances in Lung Cancer: Diagnostics, Molecular Pathways, and Emerging Therapeutic Strategies*, *Int. J. of Pharm. Sci.*, 2026, Vol 4, Issue 5, 2406-2427. <https://doi.org/10.5281/zenodo.20123652>