All About Non-Small Cell Lung Cancer

What are the lungs?

Lungs are two spongy organs located in the chest. They deliver oxygen to the bloodstream. When you take a breath in, air moves into the lungs, causing them to expand (stretch). The air comes very close to blood that is traveling in small vessels called capillaries. The lungs are designed to place blood in close contact with as much air as possible, so their tissues are very delicate. When you breathe out, you exhale (breathe out) substances that you don't need, like carbon dioxide. The right lung has three sections, called lobes; the left lung has two lobes.

You breathe in air through your mouth and nose. This air then travels down a tube, called the trachea. The trachea divides into smaller branches called bronchi, and the bronchi keep dividing and dividing like branches on a tree. As the branches get smaller, they are called bronchioles. At the end of the branches, there are little sacs of air called alveoli. The air comes into contact with blood in the alveoli. The lungs are exposed to whatever you breathe in, so any toxic chemicals or pollutants in the air you breathe can get into your body through your lungs.

What is lung cancer?

Cancer happens when cells grow in an uncontrolled way, which can lead to a tumor developing. Lung cancer occurs when cells in the lung begin to grow out of control. These cells can then spread to nearby tissues or throughout the body. Cells in any of the tissues in the lung can develop cancer. Most commonly, lung cancer comes from the lining of the bronchi. Cancers are described by the type of cells they come from. Lung cancer is divided into two main categories:

- **Small cell lung cancer (SCLC)** - the rarer of the two types (about 15% of all lung cancers), small cell lung cancer can be more aggressive than non-small cell lung cancer because it grows more quickly and is more likely to spread to other organs.
- **Non-small cell lung cancer (NSCLC)** - the more common of the two types (80-85% of all lung cancers), non-small cell lung cancer is generally slower growing than small cell lung cancer. NSCLC is divided into different types based on how the cells look that make it up - adenocarcinoma, squamous cell carcinoma, and poorly differentiated or large cell carcinoma.

What causes lung cancer and am I at risk?

There are about 235,760 new cases of lung cancer diagnosed in the United States each year. The average age of diagnosis is 71. Lung cancer is slightly more common in men than women across all racial groups. Lung cancer is the most common cause of cancer deaths.

Smoking is the greatest risk factor for developing lung cancer. Other causes of lung cancer include exposure to radon, exposure to radiation, environmental exposure to particular chemicals, and previous lung diseases.
Smoking

Every smoker (current or former) is at risk for lung cancer. Your risk of getting lung cancer from cigarette smoking increases the longer you smoke, the more you smoke, and the deeper you inhale. Smoking low tar cigarettes does not prevent you from getting lung cancer. Importantly, if you quit smoking, your risk of getting lung cancer declines. The longer you go without smoking, the greater your risk declines. It is never too late to quit because your risk declines no matter how long you have been smoking. In addition, giving up smoking decreases the chance of developing another lung cancer after treatment for the current cancer.

Those with lung cancer have been found to respond to treatment better and live longer if they quit smoking at the time of their diagnosis. If they continue to smoke, they can have a harder time getting through treatment, being at higher risk of side effects such as pneumonia and lung inflammation. This can result in needing to lower the chemotherapy doses a person receives, which can result in less effective therapy.

Smoking also has an effect on people around you. Second-hand smoke or smoke inhaled when you are near someone smoking, is another risk factor for lung cancer.

Smoking pipes and cigars is also a risk factor for lung cancer. Even though you are not inhaling, you are breathing the air that is filled with the smoke from these products. The more pipes or cigars you smoke, the more likely you are to get lung cancer. Although it is not as well established as cigarette smoking, smoking marijuana is also a risk factor for getting lung cancer. Both how much marijuana and how often you smoke it seems to be related to your overall risk.

Radon

Radon is the second leading cause of lung cancer in the United States. Radon is a naturally occurring, odorless, colorless, radioactive gas that results from the decay of rock and soil components. Radon moves up from the ground into homes, where it becomes trapped and builds up. This exposes the residents to its cancer-causing potential. Different areas of the world have different amounts of radon produced. The type of foundation in your home is also important since some foundations are better ventilated. Because of this, two homes next door to each other could have different levels of radon in the indoor air.

Radon can build up in new and old homes and those with or without a basement. The only way to know if your home contains radon is to have it tested. This can be done using a kit from a hardware store or having a radon professional perform the test. Many areas have laws requiring radon testing before a house is sold. If radon is detected in levels above 4 pCi/L (picocuries per liter), you can have a removal system installed, which vents the gas to the outside using a pipe and fan system.

Radiation Exposure

Radiation therapy used to treat a prior cancer that had the lungs in the treatment area increases the risk for developing a new cancer in that area of the lung. Such secondary cancers often take a decade or longer to develop. This can be seen in people treated for Hodgkin lymphoma and breast cancer, among others. Some guidelines suggest that Hodgkin lymphoma survivors have screening for lung cancers after treatment. Modern radiation equipment and planning reduces the exposure of healthy tissue and may reduce this risk.

Other Risk Factors

There are some environmental exposures that increase your risk for lung cancer as well. People who work with asbestos are more likely to get lung cancer; and if they smoke cigarettes too, their risk is even higher. Asbestos is found in industries like shipbuilding, insulation/fireproofing, and asbestos mining and production. Other workers who may have a higher risk of lung cancer are those exposed to arsenic, chromium, nickel, vinyl chloride, hard metal dust, talc, uranium, and gasoline and diesel exhaust fumes.

Electronic nicotine delivery systems (e-cigarettes) and hookah use are becoming more popular. At this time, there is no conclusive research stating that the use of e-cigarettes can cause lung cancer. However, the tiny particles in the aerosol of e-cigarettes can contain toxic chemicals that can penetrate into the lungs. Hookah use, and being exposed to hookah smoke, can cause serious health risks, including lung cancer. The tobacco used in a hookah is exposed to high heat from burning charcoal which is at least as toxic as cigarette smoke. The tobacco and toxic agents used in hookah can be risk factors for lung cancer.

People who have already had lung cancer are at risk of getting it again. A history of interstitial lung disease, pulmonary fibrosis,
or tuberculosis (TB) also increases your risk of getting lung cancer. Changes in your genes, both from the environment and some inherited from your parents can also increase your risk of lung cancer.

**Lung Cancer in Never Smokers**

The number of cases of lung cancer in never smokers (people who have smoked less than 100 cigarettes in their lifetime) has been increasing in many countries, including the United States. Worldwide, never smokers make up 15-20% of new lung cancer cases in men, but 50% of new cases in women. Most lung cancers in never smokers are non-small cell lung cancers, as small cell lung cancer occurs almost exclusively in current or former smokers. This makes researchers think that lung cancer in never smokers may be a biologically different disease than in smokers.

The cause of these cancers is not clear, though the risk factors discussed above are all possibilities. Researchers are studying how these cancers may respond differently to targeted therapies aimed at specific molecular abnormalities and how smoking status could be used in treatment planning.

**How can I prevent lung cancer?**

The best way to prevent lung cancer is not to smoke or to quit if you already smoke. Avoid being around people who are smoking. Do not use pipes, cigars, hookahs, or smoke marijuana. Have your home tested for radon and install a removal system if needed. If you work in an industry where you are exposed to substances known to cause lung cancer, make sure to use all the proper protective equipment and attire made available by your employer.

The future of lung cancer prevention will rely on sophisticated analysis of patients' genes and molecular markers for lung cancer risk. This coupled with "smart drug" design and new imaging techniques may one day help decrease the risk of developing lung cancer.

**What screening tests are available?**

Lung cancer screening is not suggested for those at average risk of lung cancer. Those at higher risk should talk with their healthcare providers about the US Preventive Task Force recommendations for lung cancer screening. Screening is done with a low-dose CT (LDCT) scan of your chest. Testing may be recommended for you if:

- You are between the ages of 50 to 80 and in fairly good health.
- You are currently a smoker or have quit within the past 15 years.
- You have at least a 20-pack-year smoking history (you have smoked a pack a day for 20 years or 2 packs a day for 10 years).
- You will receive smoking cessation counseling if you are a current smoker.
- You have been involved in informed/shared decision-making about the benefits, limitations, and harms of screening with LDCT scans.
- You have access to high-volume, high-quality lung cancer screening, and a treatment center.

**What are the signs of lung cancer?**

Unfortunately, the early stages of lung cancer may not have any symptoms. As the tumor grows in size, it can produce a variety of symptoms including:

- Cough (especially one that doesn't go away or gets worse).
- Chest pain.
- Shortness of breath.
- Coughing up blood or bloody phlegm.
- New hoarseness, wheezing, or changes in how your voice sounds.
- Pneumonia or bronchitis that keeps coming back.
- Weight loss.
- Loss of appetite.
- Fatigue (feeling more tired than usual).
- Bone pain, arm pain, new weakness.
- Dizziness or double vision.
- Numbness or tingling in your arms or legs.
- Neck or facial swelling.

You should see your healthcare provider if you are having any of these symptoms. Many of these symptoms can occur with other health conditions. A cough is the most common presenting symptom of lung cancer; however, many long-term smokers have a chronic cough, so it is especially important for someone with a chronic cough to see their healthcare provider if their cough changes or gets worse.

**How is lung cancer diagnosed?**

If you have symptoms of lung cancer, usually you will be referred for blood work and a chest x-ray and/or CT scan (a 3-D x-ray) of the chest. Your provider may order sputum cytology, which looks at your phlegm for cancer cells. To see if the lung cancer has spread outside of the chest (metastasis), you may have a CT scan of the abdomen (belly) and/or a PET-CT scan. To see if the lung cancer has spread to the brain, you may have an MRI or CT scan of the brain. Often times, your doctor will order tests called PFT’s (pulmonary function tests) to assess your lung capacity prior to considering surgery, radiation therapy, and some types of chemotherapy.

While all of these tests are important pieces of the puzzle, a biopsy is the only way to know for sure if you have cancer. A biopsy takes a sample of the suspicious area, which is then looked at under a microscope for any cancer cells. The biopsy is also necessary to determine the type of lung cancer and if there are cancer cells present in the lymph nodes.

A biopsy may be taken of the suspicious area in the lung and/or from lymph nodes near the lungs. Your provider will determine which areas should be biopsied and which biopsy method is best in your case. Biopsies are often done by a lung surgeon or a pulmonologist (a doctor specializing in lung diseases), who is trained in bronchoscopy. Possible methods for obtaining a biopsy include:

- **Bronchoscopy:** uses a thin, lighted tube placed down your nose or mouth and into your lung to look at the tumor and take samples of it. This can also be used to take samples of the lymph nodes. There are several bronchoscopy techniques that can be used. Your healthcare provider will determine which methods are best in your case based on the location of the lesion and if lymph nodes are being sampled.
- **Needle biopsy:** a needle is placed through the skin and between the ribs, and then into the tumor to get cells.
- **Thoracoscopic:** A surgical procedure where the surgeon inserts a small camera into the chest wall to look at the suspicious area, evaluate the extent of the tumor, and take biopsies.
- **Video-assisted thoracoscopic or VATS:** can be used for a biopsy or surgery in early-stage lung cancer; this technique is similar to thoracoscopic but requires fewer/smaller incisions, which may result in quicker recovery.
- **Mediastinoscopy:** A surgical procedure that uses a scope (camera on a tube), placed through the chest wall, to look at the suspicious area and take samples of lymph nodes to evaluate for the presence of cancer cells.

In some cases, tumor cells can get into the fluid around your lungs (called pleural fluid). Your healthcare provider may want to drain off some fluid by putting a needle into the space where the fluid has collected and examine that fluid under a microscope. This is called a thoracentesis.

Once the tissue is removed, a healthcare provider called a pathologist examines the specimen under a microscope. The pathologist determines if it is cancer or not. If it is cancerous, they will characterize it the tumor by

- What type of tissue it came from.
- What subtype of non-small cell lung cancer it is (histology)
  - Adenocarcinoma.
  - Squamous Cell Carcinoma.
  - Large Cell Carcinoma.
  - Adenosquamous Carcinoma.
  - Sarcomatoid Carcinoma.

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• How abnormal it looks (known as the grade).
• If it is invading surrounding tissues.

The pathologist sends a pathology report to your healthcare provider, detailing their findings. This is an important piece in planning your treatment. You can request a copy of your report for your records.

Genetic abnormalities have been identified in non-small cell lung cancers. These abnormalities can be used to tell us more about prognosis and/or predict how you may respond to a specific treatment. Many centers now routinely test for EGFR mutations and ALK gene rearrangements in metastatic lung cancer in never smokers. The presence of EGFR mutations is used to determine the appropriateness of using EGFR Inhibitor treatment, a type of "targeted therapy." Tumors with ALK gene rearrangements are treated with medications that target this abnormality. You may also be tested for a KRAS, ROS1, BRAF and RET mutation. Talk to your healthcare provider about molecular testing for your specific case.

If you are having particular symptoms, your provider may want different or more specific exams to determine their cause.

**How is lung cancer staged?**

After these tests are done, the stage of the cancer can be determined. Overall, your providers will want to know as much about your cancer and your health as possible so that they can plan the best available treatments. Clinical staging is done based on the size and location of the tumor on CT scans and PET scans, and if there is any evidence of spread to other organs that is seen with radiology tests. The stage of the cancer affects how it is treated.

The staging system used to describe small cell lung cancer is the “TNM system,” as described by the American Joint Committee on Cancer. The TNM systems are used to describe many types of cancers. They have three parts:

- T-describes the size/location/extent of the "primary" tumor in the lung.
- N-describes if the cancer has spread to the lymph nodes.
- M-describes if the cancer has spread to other organs (metastases).

Treatment planning for non-small cell lung cancer depends on the stage and your overall health. Some patients will be able to have surgery while others will not. Surgery, chemotherapy and radiation are all treatment options, either used alone or in different combinations. You will want to discuss your options and your goals of treatment with your team.

The staging system is very complex. The entire staging system is outlined at the end of this article. Though complicated, the staging system helps healthcare providers determine the extent of the cancer, and in turn, make treatment decisions for your cancer.

**How is lung cancer treated?**

Treatment planning for non-small cell lung cancer depends on the stage and your overall health. Some patients will be able to have surgery while others will not. Surgery, chemotherapy and radiation are all treatment options, either used alone or in different combinations. You will want to discuss your options and your goals of treatment with your team.

**Surgery**

The goal of surgery is to remove all of the cancer if possible. If the tumor is small and in a favorable location, or if you have limited lung function, the surgeon may choose to remove the tumor with a small section of lung. This is called a wedge resection. In most cases, the surgeon will choose to remove the entire lobe of the involved lung. This is known as a lobectomy. In some cases, the surgeon must remove the entire lung affected by the cancer. This is known as pneumonectomy.

Not everyone can tolerate these surgeries. Patients with limited lung function may not be able to tolerate surgery. Preoperative pulmonary function tests (PFT’s) are used to help predict who is a good candidate for surgery. Sometimes another test called a quantified ventilation perfusion scan will be ordered. This test shows the extent that each area of lung is currently working. These tests may help the surgeon predict how much lung function will be lost based on the amount of lung that will need to be removed, and how you will feel after surgery.

Another use for surgery in lung cancer is to treat metastasis. If there is one metastatic lesion to the brain or spine, a
neurosurgeon may want to remove them surgically. A solitary metastatic lesion to the adrenal gland may also be managed with surgical removal. Talk with your healthcare provider about the different ways to approach treatment of your particular disease.

Chemotherapy

Chemotherapy refers to medications to treat cancer that are usually given intravenously (IV, into a vein) or in pill form to take by mouth. Chemotherapy travels throughout the bloodstream and throughout the body to kill cancer cells. This is one of the big advantages of chemotherapy. If cancer cells have broken off from the tumor and are somewhere else inside the body, chemotherapy has the chance of killing them, while radiation does not.

Chemotherapy and radiation may be given at the same time. This is called concurrent chemoradiation. In this case, the chemotherapy not only treats the cancer, but also works as a "radiosensitizer," making the tissues more sensitive to radiation, helping the therapy be more effective.

Different chemotherapy regimens are used for different patients, based on the type of lung cancer, side effect profile of the medication and the goal of treatment. Some of the chemotherapy agents used include: cisplatin, carboplatin, pemetrexed, paclitaxel, docetaxel, durvalumab, etoposide, gemcitabine, and vinorelbine.

There are advantages and disadvantages to each of the different regimens that your healthcare provider will discuss with you. Based on your own health, your personal values and wishes, and side effects you may wish to avoid, you can work with your healthcare team to come up with the best regimen for your cancer and your lifestyle.

Targeted Therapies/Biologic Therapies

Researchers are studying a variety of biomarkers that can be measured in the patient or the tumor. Biomarkers can be used to determine the potential benefit (or lack thereof) of chemotherapy or how well a certain treatment will work. This is often described as "personalized medicine." This means the treatment is no longer just based on the cancer type, but is much more specific to the genetic make-up of a patient's tumor. Much of this shift in treatment decisions is possible because of targeted therapies.

Cancers have abnormal genetic pathways and receptors, some of which have been identified by researchers and in some cases, can be detected with laboratory tests. These abnormal pathways and receptors allow cells to become cancerous and/or resistant to treatment with chemotherapy and radiation therapy. These changes in the genes and pathways are called genetic mutations. Targeted (also called "biologic") therapies are a class of medications that have been designed to target certain genetic mutations in various cancers. These medications often produce very different side effects than standard chemotherapy and can be given alone or in combination with standard chemotherapy.

Targeted therapies used in the treatment of specific genetic mutations include:

- EGFR positive: Afatinib, erlotinib, dacomitinib, gefitinib, ramucirumab, bevacizumab and osimertinib.
- ALK positive: Alectinib, brigatinib, ceritinib, crizotinib and lorlatinib.
- ROS1 positive: Ceritinib, entrectinib, lorlatinib and crizotinib.
- BRAF V600E positive: Dabrafenib and trametinib.
- RET Rearrangement positive: Selpercatinib, pralsetinib, cabozantinib, vandetanib.
- MET Exon 14 Skipping mutation: Crizotinib, capmatinib, tepotinib.
- ERBB (HER2) mutations: Ado-tratuzumab emtansine, fam-trantuzumab deructecan-nxki.
- NTRK Gene Fusion positive: Larotrectinib, entrectinib.
- PD1 positive: Pembrolizumab, bevacizumab, nivolumab, illimumab, cemiplima-rwlc and atezolizumab. These PD1 medications are immunotherapies. This means they stimulate the body's own immune system to target and destroy cancer cells.

One type of targeted therapy is an anti-angiogenesis agent, which targets receptors on blood vessels, inhibiting the growth of new blood vessels, in turn slowing tumor growth by cutting off its blood supply. Bevacizumab and ramucirumab are anti-angiogenesis agents used in lung cancer treatment.

Radiation
Radiation therapy, given after or concurrently with chemotherapy, is the most commonly used treatment for locally advanced lung cancer. Radiation therapy may be recommended before surgery to shrink a tumor to make it easier for the surgeon to remove. Radiation therapy may be used after surgery to help prevent recurrence (the cancer coming back) in the chest. Radiation therapy can be used instead of surgery if a surgery is felt to be too dangerous for the patient, or if a tumor is too extensive to be removed with surgery. Radiation therapy uses high-energy rays (similar to x-rays) to kill cancer cells and is commonly used to treat lung cancer. Radiation therapy is given using a machine called a linear accelerator. Your treatment plan, including how long and how often you will be treated, will be determined by your treatment team. The treatment takes just a few minutes and is painless.

**Radiation for Metastatic Disease**

Radiation can also be used when the cancer has spread to other parts of the body, including the bones, spine and brain. Radiation can be used to reduce pain from metastatic disease, or to reduce the risk of problems from cancer that has spread to the brain or spine.

**Stereotactic Radiation**

Stereotactic radiation, often referred to as stereotactic body radiation therapy (SBRT) or stereotactic ablative body radiotherapy (SABR), is a form of radiation therapy that very precisely delivers a high dose of radiation therapy to a tumor. SBRT differs from standard radiation therapy, in that it involves fewer treatments; often 1-5 treatments over 1-2 weeks, compared with the 6-8 week regimens with conventional radiation therapy. Although SBRT involves fewer treatment sessions (fractions), the radiation dose delivered during each fraction is much higher than conventional radiation therapy. Since the dose per day of radiation therapy is so high, the radiation oncologist must very precisely target the location of the tumor. In order to do this, SBRT functions like a magnifying glass, delivering radiation therapy from different angles to focus the irradiation at one small point where the beams converge. The use of multiple unique beam angles or arcs limits dose to the surrounding normal tissue.

SBRT to the lung is often delivered with either CyberKnife® or Linac-based SBRT. The location and size of tumors is very important in selecting this treatment method, as tumors in the wrong location can put patients at increased risk for serious side effects. For example, if a tumor is very close to the trachea (windpipe), patients can experience damage to these areas and may not be good candidates for this treatment.

**Photodynamic Therapy**

Photodynamic therapy (PDT) is a treatment that uses light to damage malignant or abnormal tissues. PDT is FDA-approved for providing relief of obstruction caused by (NSCLC). PDT uses a light source, such as a laser, combined with a medication that makes the tissues light-sensitive, which is known as a "photosensitizer." When the light and photosensitizer are combined, oxygen-free radicals that can destroy cancer cells are released. Photosensitizers are often taken up in greater amounts by cancer cells compared to normal cells.

A photosensitizing drug is given to the patient a few hours to a few days prior to the light exposure, but the medication is not activated until it is exposed to a particular wavelength of light. When the light is directed at the area of the cancer, the photosensitizer is activated and the cancer cells are destroyed. This wavelength determines how far the light can travel into the body. Typically, the depth of penetration is in millimeters. Therefore, PDT is generally not used to treat large tumors, because the light cannot reach the necessary depth to treat those tumors. Different photosensitizers are activated by different wavelengths of light; therefore, depending on the area of the body to be treated, there are different photosensitizing drugs and different wavelengths of light that can be used.

**Clinical Trials**

Clinical trials are extremely important in furthering our knowledge of this disease. It is through clinical trials that we know what we do today, and many exciting new therapies are currently being tested. Talk to your healthcare provider about participating in clinical trials in your area. You can also explore currently open clinical trials using the [OncoLink Clinical Trials Matching Service](http://www.oncolink.org).

**Follow-up Care and Survivorship**

Once you have been treated for lung cancer, you will need to be closely followed by your oncology team. At first, you will have
follow-up visits fairly often. The longer you are free of disease, the less often you will have to go for checkups. Specific recommendations on how often you should be seen by your provider and have a chest CT depend on the stage of cancer you had and the treatments you received. Often, for patients with Stage I or II treated with surgery and chemotherapy, it is recommended to have an assessment done by a provider, including a chest CT, every 6 months for the first 2-3 years and then annually. For patients Stage I-II treated with radiation or Stages III-IV, it is recommended to have an assessment and chest CT done every 3-6 months for 3 years, every 6 months for 2 years and then annually. It is also suggested that an annual flu vaccine, herpes zoster and pneumococcal vaccination be given.

If you are a smoker, quitting smoking is important in lung cancer survivorship. Remember, it is never too late to get the health benefits of smoking cessation. If your family members smoke, it is a great opportunity to support each other and quit together. There are many programs to provide support in quitting as well as medications to support your efforts.

Fear of recurrence, relationship challenges, financial impact of cancer treatment, employment issues and coping strategies are common emotional and practical issues experienced by lung cancer survivors. Your healthcare team can identify resources for support and management of these practical and emotional challenges faced during and after cancer.

Cancer survivorship is a relatively new focus of oncology care. With nearly 17 million cancer survivors in the US alone, there is a need to help patients transition from active treatment to survivorship. What happens next, how do you get back to normal, what should you know and do to live healthy going forward? A survivorship care plan can be a first step in educating yourself about navigating life after cancer and helping you communicate knowledgeably with your healthcare providers. Create a survivorship care plan today on OncoLink.

**Resources for More Information**

**Go2 Foundation for Lung Cancer**

Provides support and advocacy for people living with lung cancer or at risk for the disease.

https://go2foundation.org

**Lungevity**

Dedicated to changing outcomes for people with lung cancer through research, education, and support.

http://lungevity.org/

**American Lung Association**

Information on diagnosis, treatment and support.


**Free to Breathe**

Funds research and advocates for improved treatments. Provides patients with treatment information.

http://www.freetobreathe.org/

**Lungcancer.org**

Professional oncology social workers provide free emotional and practical support for people with lung cancer, caregivers, and their loved ones; affiliated with CancerCare.

http://www.lungcancer.org/

**Appendix: Complete Lung Cancer Staging**

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<table>
<thead>
<tr>
<th>Primary Tumor (T)</th>
<th>Description</th>
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<tbody>
<tr>
<td>TX</td>
<td>Primary tumor cannot be assessed, or tumor proven by the presence of malignant cells in sputum or bronchial washing but not visualized by imaging or bronchoscopy</td>
</tr>
<tr>
<td>T0</td>
<td>No evidence of primary tumor</td>
</tr>
</tbody>
</table>
| T1s              | Carcinoma in situ  
Squamous cell carcinoma in situ  
Adenocarcinoma in situ: adenocarcinoma with pure lepidic pattern, ≤ 3 cm in greatest dimension |
| T1               | Tumor ≤ 3 cm in greatest dimension, surrounded by lung or visceral pleura, without bronchoscopy evidence of invasion more proximal than the lobar bronchus (i.e. not in the main bronchus) |
| T1mi             | Minimally invasive adenocarcinoma: adenocarcinoma (≤ 3 cm in greatest dimension) with a predominantly lepidic pattern and ≤5 mm invasion in greatest dimension |
| T1a              | Tumor ≤ 1 cm in greatest dimension. A superficial, spreading tumor of any size whose invasive component is limited to the bronchial wall and may extend proximal to the main bronchus also is classified as T1a, but these tumors are uncommon. |
| T1b              | Tumor > 1 cm but ≤ 2 cm in greatest dimension |
| T1c              | Tumor > 2 cm but ≤ 3 cm in greatest dimension |
| T2               | Tumor > 3 cm but ≤ 5 cm or tumor with any of the following features: (1) Involves the main bronchus, regardless of distance to the carina, but without involvement of the carina; (2) Invades visceral pleura (PL1 or PL2); (3) Associated with atelectasis or obstructive pneumonitis that extends to the hilar region, involving part or all of the lung |
| T2a              | Tumor > 3 cm but ≤ 4 cm in greatest dimension |
| T2b              | Tumor ≥ 4 cm but ≤ 5 cm in greatest dimension |
| T3               | Tumor > 5 cm but ≤ 7 cm in greatest dimension or directly invades any of the following: parietal pleura, chest wall, phrenic nerve, parietal pericardium; or separate tumor nodule(s) in the same lobe as the primary |
| T4               | Tumor > 7 cm or of any size that invades any of the following: diaphragm, mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, esophagus, vertebral body, carina; separate tumor nodule(s) in an ipsilateral lobe different from that of the primary |

<table>
<thead>
<tr>
<th>Regional Lymph Nodes (N)</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>NX</td>
<td>Regional lymph nodes cannot be assessed</td>
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<tr>
<td>N0</td>
<td>No regional lymph node metastasis</td>
</tr>
<tr>
<td>N1</td>
<td>Metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary nodes, including involvement by direct extension</td>
</tr>
<tr>
<td>N2</td>
<td>Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s)</td>
</tr>
<tr>
<td>N3</td>
<td>Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph node(s)</td>
</tr>
</tbody>
</table>

<p>| Distant Metastasis (M) | Description |</p>
<table>
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<th>MX</th>
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</tr>
</thead>
<tbody>
<tr>
<td>M0</td>
<td>No distant metastasis</td>
</tr>
<tr>
<td>M1</td>
<td>Distant metastasis</td>
</tr>
<tr>
<td>M1a</td>
<td>Separate tumor nodule(s) in a contralateral lobe; tumor with pleural nodules or malignant pleural (or pericardial) effusion</td>
</tr>
<tr>
<td>M1b</td>
<td>Single extra thoracic metastasis in a single organ (including involvement of a single nonregional node)</td>
</tr>
<tr>
<td>M1c</td>
<td>Multiple extrathoracic metastases in a single organ or in multiple organs</td>
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<thead>
<tr>
<th>Prognostic Groups</th>
<th>T</th>
<th>N</th>
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<tr>
<td>Occult Carcinoma</td>
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<td>M0</td>
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<tr>
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<td>M0</td>
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<td>M0</td>
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<tr>
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