Understanding Your Pathology Report: Lung Cancer

When your lung was biopsied, the samples taken were studied under the microscope by a specialized doctor with many years of training called a pathologist. The pathologist sends your doctor a report that gives a diagnosis for each sample taken. Information in this report will be used to help manage your care. The questions and answers that follow are meant to help you understand medical language you might find in the pathology report you received after your lung biopsy.

The information that would be in a pathology report based on having all or part of your lung removed (resected) as a treatment for lung cancer is not covered here.

What is the normal structure of the lung?

When you breathe in, air enters through your mouth or nose and goes into your lungs through the trachea (windpipe). The trachea divides into 2 tubes called the bronchi (singular, bronchus), which divide into smaller branches called bronchioles. At the end of the bronchioles are tiny air sacs known as alveoli or acini.

Many tiny blood vessels run through the alveoli. They absorb oxygen from the inhaled air into your blood and pass carbon dioxide from the body into the alveoli. This is expelled from the body when you breathe out. Taking in oxygen and getting rid of carbon dioxide are your lungs’ main functions.

What is carcinoma?

Carcinoma is a type of cancer that starts in the cells that line organs. In the lung, carcinomas can start in the cells that line the inside of the bronchi, bronchioles, and alveoli. Carcinoma is the most common kind of lung cancer\(^1\). In fact, when someone
says they have lung cancer, they usually mean that they have a carcinoma.

What does infiltrating or invasive mean?

Carcinomas can start in the cells that line the inside of the bronchi, bronchioles, or alveoli. If the carcinoma cells are only in the top layer of cells lining these structures, it is called in-situ carcinoma (or carcinoma in situ). This is considered a pre-cancer.

When carcinoma cells grow into the deeper layers of the lung, it is called invasive or infiltrating carcinoma. At this point the cancer cells can spread (metastasize) outside of the lung to lymph nodes and other parts of your body. Invasive carcinomas are considered true lung cancers and not pre-cancers.

What does it mean if my carcinoma is called squamous carcinoma or squamous cell carcinoma?

Carcinomas are named based on how the cells look under the microscope. Squamous carcinoma or squamous cell carcinoma is the name of a type of non-small cell lung cancer where the cells resemble the flat cells (called squamous cells) that line the airways. It is a common type of lung cancer in the United States.

What does it mean if my carcinoma is called adenocarcinoma?

Carcinomas are named based on how the cells look under the microscope. Adenocarcinoma is a type of non-small cell lung cancer where the cells resemble gland cells, such as the glands that secrete mucus in the lungs. This is the most common type of lung cancer in the United States.

What does it mean if the following terms are used to describe the adenocarcinoma: papillary, micropapillary, acinar, mucinous, or solid?

These terms describe different types of lung adenocarcinoma, which are based on how the cells look and are arranged under the microscope (called growth patterns). Some tumors look basically the same throughout the tumor, and some can look different in different areas of the tumor. Some growth patterns have a better prognosis (outlook) than others. Since some tumors can have a mixture of patterns, the pathologist can’t always tell all the types contained in a tumor just based on a biopsy that samples only a small part of the tumor. To know what types a tumor contains, the entire tumor must be removed.

What does it mean if my carcinoma is called small cell carcinoma?
Small cell carcinoma (also known as small cell lung cancer) is a special type of lung cancer that tends to grow and spread quickly. Since it has often spread outside the lung at the time it is diagnosed, it is rarely treated with surgery. It is most often treated with chemotherapy, which might be combined with radiation. The chemotherapy used is different from what is used for other types of lung cancers.

What does it mean if my carcinoma is called non-small cell carcinoma?

In some cases, the cancer clearly does not look like small cell carcinoma under the microscope, but at the same time it is hard to tell whether it is a squamous cell carcinoma or adenocarcinoma. This distinction between squamous cell carcinoma and adenocarcinoma may be especially difficult in small biopsy specimens. The term non-small cell carcinoma is often used for these carcinomas until they can be more precisely classified by special lab tests (such as immunohistochemistry), or until the entire tumor is removed during surgery and then examined.

What does it mean if my carcinoma is well differentiated, moderately differentiated, or poorly differentiated?

These terms are assigned by a pathologist based on how the cancer cells look under the microscope:

- **Well-differentiated carcinomas** tend to look a lot like the type of cells from which they arose.
- **Moderately differentiated carcinomas** retain only some of the features of the cells from which they arose.
- **Poorly differentiated carcinomas** look very different from the cells from which they arose.

Unlike carcinomas that start in organs such as the breast, prostate, and kidney, the differentiation (grade) of a lung carcinoma has not been shown to be helpful in predicting a person’s prognosis (outlook).

What does it mean if my report says typical carcinoid or atypical carcinoid tumor?

**Carcinoid tumors** are a special type of tumor. They start from cells of the diffuse neuroendocrine system. This system is made up of cells that are like nerve cells in certain ways and like hormone-making endocrine cells in other ways. These cells do not form an actual organ like the adrenal or thyroid glands. Instead, they are scattered
throughout the body in organs like the lungs, stomach, and intestines.

Like most cells in your body, the lung neuroendocrine cells sometimes go through certain changes that cause them to grow too much and form tumors. These are known as neuroendocrine tumors or neuroendocrine cancers. (Neuroendocrine cells in other parts of the body can also form tumors and cancers.) There are 4 types of neuroendocrine lung tumors:

- Typical carcinoid tumor
- Atypical carcinoid tumor
- Small cell carcinoma (small cell lung cancer)
- Large cell neuroendocrine carcinoma

**Typical carcinoid tumors** of the lungs are not linked to smoking. They tend to be slow growing, and only rarely spread outside the lungs.

**Atypical carcinoid tumors** grow a little faster and are somewhat more likely to spread to other organs. Seen under a microscope, they have more cells in the process of dividing and look more like a fast-growing tumor. They are much less common than typical carcinoids. Some of the features of an atypical carcinoid that may be mentioned in your report include: mitotic figures or mitoses (an indication of how fast the tumor is growing) and necrosis (when areas of the tumor are dead).

Some carcinoid tumors can release hormone-like substances into the bloodstream, which might cause symptoms. Lung carcinoids do this far less often than carcinoid tumors that start in the intestines.

**What is vascular, lymphatic, angiolymphatic, or lymphovascular invasion? What if my report mentions D2-40 (podoplanin) or CD34?**

Tumors can grow into small blood vessels and/or lymphatic vessels. When this is seen under the microscope it is called vascular, lymphatic, angiolymphatic or lymphovascular invasion. If cancer is present in these vessels it means there is a higher chance that the cancer has spread outside the lung, although this does not always occur.

D2-40 and CD34 are special tests the pathologist may use to help identify vascular, lymphatic, lymphovascular, or angiolymphatic invasion. These tests are not needed for every patient. How the presence of this finding might affect your treatment is best discussed with your doctor.

**What is the significance of the reported size of the tumor?**
If the entire tumor is removed, the pathologist will measure its size by looking at it (called the *gross examination*), or, if it is very small, measure it under the microscope. Often, what is reported is how big across it is in the area where the tumor is the largest. This is called the *greatest dimension* of the tumor, as in “the tumor measured 2 centimeters (cm) in greatest dimension.” In general, smaller tumors have a better prognosis (outlook).

A biopsy of a tumor only samples a part of the tumor, so measurements of its overall size cannot be reported.

**What is the significance of the stage of the cancer?**

The stage of the cancer is a measurement of the extent of cancer growth, including its spread to other parts of the body. To know the stage of a lung cancer, you need information on the size of the tumor in the lung and if the cancer is growing into any nearby organs or structures. You also need to know if the cancer has spread to any nearby lymph nodes or to distant sites.

Each of these pieces of information is represented by a letter:

- **T** stands for the main (primary) *tumor*.
- **N** stands for spread to nearby lymph *nodes*.
- **M** is for *metastasis* (spread) to distant parts of the body.

Once the T, N, and M categories are determined, they are combined to create an overall stage, which is given a number of I to IV (and sometimes followed by a letter), with a higher number meaning larger extent or spread of disease.

Staging information cannot usually be given for a biopsy specimen, because the pathologist needs to have the entire tumor and nearby lymph nodes to evaluate.

When this information is obtained by removing the tumor and nearby lymph nodes at *surgery*, a lower-case letter “p” is put before the T and N. So, in your pathology report, pT would be followed by numbers and letters based on the size of the tumor and some other information about it. The larger the number, the more advanced the cancer. pN followed by numbers and letters is based on the extent of spread to nearby lymph nodes that may have been removed at the same time as the lung tumor.

The pathologist does not report the M category, as they cannot determine whether there is spread to distant parts of the body just based on surgery to remove a lung tumor and nearby lymph nodes. The M category is often based on the results of imaging tests,
such as CT scans, MRIs, and bone scans, sometimes along with a biopsy of an area of suspected cancer spread.

This staging system is used for many types of lung cancer, such as adenocarcinoma, squamous cell carcinoma, and large cell carcinoma. These types of lung cancer are often grouped together as non-small cell lung cancer. This staging system also can be used to stage carcinoid tumors, but is not often used to stage small cell carcinomas of the lung.

Discuss how the stage of your tumor will affect your treatment with your doctor.

**What does it mean if in addition to a diagnosis of cancer, my report also says atypical adenomatous hyperplasia, squamous dysplasia, or squamous cell carcinoma in situ (CIS)?**

All of these are terms for pre-cancers that can be found in the lung. They are sometimes found near invasive cancer. If they are found on needle biopsy in addition to invasive cancer, it isn’t really important. If they are found in a specimen from surgery to remove the entire tumor, they may be important if they are found at or near a margin (discussed below).

**What if my report mentions margins?**

The margin is the edge or the boundary of the specimen that was removed by the surgeon. It is where the surgeon has sectioned across the lung to remove the tumor.

The margin may be free of the tumor; that is, a rim of uninvolved tissues may surround the tumor, indicating that the tumor has been removed completely. This is sometimes referred to as a negative margin.

Alternatively, the tumor could extend to the edge of the specimen (the margin), implying that the tumor has not been completely removed. This is sometimes referred to as a positive margin.

The status of the margin is an important indicator of the potential for the tumor to recur (come back) and of the need for further treatment. Talk with your doctor about the best approach for you if cancer (or pre-cancer) is found at the margins.

**What does it mean if my report mentions special tests such as p63, p40, cytokeratin 5/6 (CK5/6), TTF-1, and/or napsin A?**

p63, p40, cytokeratin 5/6, TTF-1, and napsin A are special tests that the pathologist sometimes uses to help tell adenocarcinoma from squamous cell carcinoma.

What does it mean if my report mentions special tests such as CK7 (cytokeratin 7), CK20, CDX2, gross cystic duct fluid protein (GCDFP), mammaglobin, estrogen receptor (ER), or progesterone receptor (PR), along with TTF-1?

These tests are sometimes used to help determine if a cancer in the lung started there (is a primary lung cancer) or if it spread there from somewhere else (is a metastasis). Not all patients need these tests, so if your report does not mention them, it doesn’t mean there is a problem or a question about your diagnosis.

What does it mean if my report mentions special tests such as CD56, chromogranin, or synaptophysin?

These tests are sometimes used to help see if a lung cancer is a small cell carcinoma (small cell lung cancer). They can also be helpful in diagnosing a typical carcinoid or atypical carcinoid tumor.

What does it mean if my report mentions special tests such as D2-40 (podoplanin), calretinin, WT-1, BAP-1, CEA, cytokeratin (CK) 5/6, HBME-1, Ber-EP4, TTF-1, and/or CD15 (LeuM1)?

These tests are sometimes used to help see if a tumor that includes the surface of the lung is a mesothelioma (see below) or an adenocarcinoma of the lung.

What if my report mentions EGFR, K-RAS, ALK, BRAF, or ROS1?

These are tests done to look for specific gene changes in non-small cell lung cancer cells that might affect how the cancer is best treated. These tests can help tell if you might benefit from treatment with a targeted therapy drug. How the results of your tests might affect your treatment is best discussed with your doctor.

What if my report mentions PD-L1?

This test is done to look for the PD-L1 protein on non-small cell lung cancer cells. It can help tell if you might benefit from treatment with an immunotherapy drug. How the results of your tests might affect your treatment is best discussed with your doctor.

What does it mean if my cancer is called malignant mesothelioma?
Mesotheliomas are not technically lung cancers, because they don’t develop from cells in the lung. They come from the lining on the outside of the lung, called the pleura. These cancers are not carcinomas.

Mesotheliomas are often described based on how they look under the microscope with terms like epithelial, spindled, sarcomatoid, or mixed epithelial and spindle cell features. Mesotheliomas may be linked to exposure to asbestos.

What does it mean if my report says that there is metastatic carcinoma to the lung?

Cancers that start in other organs often spread (metastasize) to the lung. Cancers that spread to the lung are still named after where they started — they are not considered lung cancers. For example, if an adenocarcinoma of the colon (colon cancer) spreads to the lung it is still a colon cancer, and not a lung cancer. This is important because chemotherapy for an adenocarcinoma of the lung is different from that used for adenocarcinoma of the colon.

What does it mean if my report also has any of the following terms: scarring, emphysema, emphysematous changes, or inflammation?

All of these are terms for non-cancerous changes that the pathologist may see under the microscope. They are usually not important when seen on a biopsy or resection that also contains cancer.

What if my report mentions any of the following: granulomas, methenamine silver (GMS), acid fast bacilli (AFB), or Periodic Acid Schiff (PAS)?

Granulomas are structures seen under the microscope that are often, although not always, caused by certain types of infections. Sometimes, the germs causing the infection can only be seen with special stains (such as GMS, stains for AFB, and PAS) that the pathologist applies to the microscopic slides.

Most granulomas are caused by infections, but other things can cause them, too, such as a disease called sarcoidosis, allergic reactions, and dust-induced lung disease (pneumoconiosis).

Hyperlinks

2. www.cancer.org/cancer/lung-cancer/detection-diagnosis-staging/how-
diagnosed.html

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Written by

This series of Frequently Asked Questions (FAQs) was developed by the Association of Directors of Anatomic and Surgical Pathology to help patients and their families better understand what their pathology report means. These FAQs have been endorsed by the College of American Pathologists (CAP) and reviewed by the American Cancer Society.

Learn more about the FAQ Initiative [www.cancer.org/treatment/understanding-your-diagnosis/tests/understanding-your-pathology-report/faq-initative-understanding-your-pathology-report.html][10]