

Nomenclature and morphological features of tumors derived from epithelium

Pretumor process

- The first step toward neoplasia is cellular transformation. Here, there is metaplasia of normal respiratory laryngeal epithelium on the right to squamous epithelium on the left in response to chronic irritation of smoking.
- The two forms of cellular transformation that are potentially reversible, but may be steps toward a neoplasm, are:
 - Metaplasia: the exchange of normal epithelium for another type of epithelium. Metaplasia is reversible when the stimulus for it is taken away.
 - Dysplasia: a disordered growth and maturation of an epithelium, which is still reversible if the factors driving it are eliminated.
- This biopsy of the lower esophagus in a patient with chronic gastroesophageal reflux disease shows columnar metaplasia (Barrett's esophagus), and the goblet cells are typical of an intestinal type of epithelium. Squamous epithelium typical of the normal esophagus appears at the right.
- This is the next step toward neoplasia. Here, there is normal cervical squamous epithelium at the left, but dysplastic squamous epithelium at the right. Dysplasia is a disorderly growth of epithelium, but still confined to the epithelium. Dysplasia is still reversible.
- At high magnification, the normal cervical squamous epithelium at the left merges into the dysplastic squamous epithelium at the right in which the cells are more disorderly.

■ Some epithelia are accessible enough, such as the cervix, that cancer screening can be done by sampling some of the cells and sending them to the laboratory. Here is a cervical Pap smear in which dysplastic cells are present that have much larger and darker nuclei than the normal squamous cells with small nuclei and large amounts of cytoplasm.

tumors derived from epithelium

- Epithelial tumors are divided in two groups:
 - benign and
 - malignant.

Classification of Epithelial tumors.

- Depending on histogenesis we differentiate:
 - - tumors of covering epithelium (multilayer, flat and transitional) and
 - - glandular epithelium.
- By their course and differentiation epithelial tumors could be
 - non-malignant (benign) and
 - malignant.
- Depending on organ specificity epithelial tumors are divided into
 - organ specific tumors and
 - tumors without specific localization.

Non-malignant Epithelial tumors

- without characteristic localization of covering epithelium - ***papillomas***
- They are found in skin,
- larynx,

- urinal bladder, etc.,
- of *glandular epithelium* – **adenomas**
- are found in all glandular organs.

Adenoma

- Adenoma - this is the epithelial tumor forming glandular patterns as well as the tumors derived from the glands but not necessarily reproducing glandular patterns.
- Benign epithelial neoplasms producing microscopically or macroscopically visible finger-like or warty projections from the epithelial surfaces are referred to as papillomas.

adenoma

- Those which form large cystic masses, as in the ovary, are referred to as **cystadenomas**.
- Some tumors produce papillary patterns that protrude into cystic spaces and are called **papillary cystadenoma**.

Morphologic variants of adenomas

- The following *morphologic variants of adenomas* are differentiated: acinous (alveolar),
- tubular,
- trabecular,
- solid,
- pappiloma cystoadenoma,
- villous adenoma,
- fibroadenoma.

polyp

- When a neoplasm, benign or malignant produces a macroscopically visible projection above a mucosal surface and projects, for example, into a gastric or colonic lumen, it is termed as polyp.
- The term "polyp" is preferably restricted to benign tumors.
- Malignant polyps are better designated as polypoid cancers.

Malignant epithelial tumors

- are called **cancer** or **carcinoma**.
- The following forms of *carcinoma without specific licalization* are differentiated:
- epidermoid cancer, developing from multilayer flat epithelium and
- is found in corresponding tissues or in mucus tunics where squamous cell metaplasia occurred.

Malignant epithelial tumors

- Malignant neoplasms of epithelial cell origin are called carcinomas.
- One within glandular growth pattern microscopically is termed as adenocarcinoma and one producing recognizable squamous cell arising in any epithelium of the body would be termed a squamous cell carcinoma.
- It is further common practice to specify, when possible, the organ of origin (renal cell adenocarcinoma, or bronchogenic squamous cell carcinoma, etc.).
- Not infrequently, however, a cancer is composed of undifferentiated cells and must be designated merely as a poorly differentiated or undifferentiated malignant tumor.

Carcinomas

- Carcinomas** could be
- high differentiated*. Cancerous keratin perls presence is characteristic for high differentiated carcinomas.
- *moderate differentiated* and
- *poorly differentiated*.

Squamous cell carcinoma of skin without keratinization.

■Epithelial cells with hyperchromic nuclei are seen, they ingrow deep into adjacent tissue. Cellular atypia is seen in epithelial cells as well as numerous mitoses.

Squamous cell carcinoma of skin with keratinization

■Epithelial cells with hyperchromic nuclei are seen, they ingrow deep into derma and adjacent tissue. Among cells with hyperchromic nuclei round shape formations are seen of homogenous red color – epithelial cancerous perls.

THE MOST IMPORTANT HUMAN TUMORS

- Here the tumors of lungs,
- stomach,
- cervix, uterus
- and breast will be discussed.

TUMORS OF THE LUNG.

- A variety of benign and malignant tumors may arise in the lung,
- but the vast majority (90 - 95 %) are **bronchogenic carcinomas**, that in industrial countries are called "public enemy number one" among all cancers.

TUMORS OF THE LUNG.

■There are some factors that play an important role in etiology and pathogenesis of this tumor: tobacco smoking, industrial hazards (radiation, asbestosis, nickel, etc.), air pollution, genetic factors, etc.

TUMORS OF THE LUNG.

■**Role of Tobacco Smoking.**

■The evidence provided by statistical and clinical observations establishing a positive relationship between tobacco smoking and lung cancer is incontrovertible. Experimental data have also been pursued, but this approach is limited by species differences.

TUMORS OF THE LUNG

■**Role of Industrial Hazards.**

■Certain industrial exposures increase the risk of developing lung cancer. All types of radiation may be cancerogenic. The risk of cancer is increased with asbestos. Among asbestos workers, one death in five is due to bronchogenic carcinoma, one in ten to pleural or peritoneal mesotheliomas, and one in ten to gastrointestinal carcinomas.

■There is also an increased risk of respiratory cancer among persons who work with nickel, chromates, coal, mustard gas, arsenic, beryllium, and iron and in newspaper workers, African gold miners, and other workers.

TUMORS OF THE LUNG

■**Role of Air Pollution.** Unquestionably, we all "swim" in a sea of carcinogens, and it is conceivable that atmospheric pollutants may play some role in the increased incidence of bronchogenic carcinoma today. Recent attention has been drawn to the potential problem of "indoor" air pollution.

■**Role of Genetic Factors.** Occasional familial clustering has suggested a genetic predisposition to lung cancer, as has the variable risk even among very heavy smokers. However, attempts at defining markers of genetic susceptibility have proved elusive.

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CLASSIFICATION TUMORS OF THE LUNG

■. Numerous histologic classifications of bronchogenic carcinoma have been proposed, but the currently popular ones, based on classifications of the World Health Organization, divide these tumors into

■**four major categories:**

- squamous cell carcinoma, and
- adenocarcinoma of approximately equal frequency, 25 to 40 % each;
- small cell carcinoma, 20 to 25 %; and

- large cell carcinoma, 10 to 15%.

CLASSIFICATION TUMORS OF THE LUNG

- There may be mixtures of histologic patterns, even in the same cancer.
- Thus combined types of squamous cell carcinoma and adenocarcinoma or
- of small cell and squamous cell carcinoma are not infrequent. Another classification in common clinical use is based on response to available therapies:
- small cell carcinomas (high initial response to chemotherapy) versus non-small cell carcinomas (less responsive). The strongest relationship to smoking is with squamous cell and small cell carcinoma.
- From a histogenetic point of view, it seems most likely that all histologic variants of bronchogenic carcinoma, including small cell carcinoma as well as the bronchial carcinoid are derived from endoderm or a derivative - a view consistent with the frequency of tumors with mixed histologic patterns.

MORPHOLOGY TUMORS OF THE LUNG

- Bronchogenic carcinomas arise most often in and about the hilus of the lung. About three-fourths of the lesions take origin from first-, second-, and third-order bronchi.
- A small number of primary carcinomas of the lung arise in the periphery of the lung substance from the alveolar septal cells or terminal bronchioles. These are predominantly **adenocarcinomas**, including those of the **bronchioloalveolar type**, to be discussed separately.

MORPHOLOGY TUMORS OF THE LUNG

- Carcinoma of the lung begins as an area of in situ cytologic atypia that, over an unknown interval of time, yields a small area of thickening or piling up of bronchial mucosa. With progression, this small focus, usually less than 1 cm in area, assumes the appearance of an irregular, warty excrescence that elevates or erodes the lining epithelium.

MORPHOLOGY TUMORS OF THE LUNG

- The tumor may then follow variety of paths.
- It may continue to fungate in to the bronchial lumen to produce an intraluminal mass.
- It can also rapidly penetrate the wall of the bronchus to infiltrate along the peribronchial tissue into the adjacent region of the carina or mediastinum.
- In other instances, the tumor grows along a broad front to produce cauliflower-like intraparenchymal mass that appears to push lung substance ahead of it. In almost all patterns, the neoplastic tissue is gray-white one, firm to hard.

MORPHOLOGY TUMORS OF THE LUNG

- Especially when the tumors are bulky focal areas of hemorrhage or necrosis may appear to produce yellow-white mottling and softening. Sometimes these necrotic foci cavitate.
- Extension may occur to the pleural surface and then within the pleural cavity or into the pericardium. Spread to the tracheal, bronchial, and mediastinal nodes can be found in most cases. The frequency of nodal involvement varies slightly within the histologic pattern but averages over 50 %.

MORPHOLOGY TUMORS OF THE LUNG Squamous Cell Carcinoma

- This type is most commonly found in men and is closely correlated with a smoking history.
- The microscopic features are familiar in the form of production of keratin and intercellular bridges in the well-differentiated forms, but many less well-differentiated squamous cell tumors are encountered that begin to merge with the undifferentiated large cell pattern. This tumor arises in the larger, more central bronchi, tends to spread locally, and metastasizes somewhat later than the other patterns, but its rate of growth in its site of origin is usually more rapid than that of other types.
- Squamous metaplasia, epithelial dysplasia, and foci of frank carcinoma in situ are sometimes present in bronchial epithelium adjacent to the tumor mass.

This is a squamous cell carcinoma of the lung that is arising centrally in the lung (as most squamous cell carcinomas do). It is obstructing the right main bronchus. The neoplasm is very firm and has a pale white to tan cut surface.

MORPHOLOGY TUMORS OF THE LUNG Adenocarcinoma

■Histologic classifications of adenocarcinomas include at least two forms:

- 1) the usual bronchial-derived adenocarcinoma and
- 2) a somewhat distinctive type termed bronchioloalveolar carcinoma, which probably arises from terminal bronchioles or alveolar walls. There may be overlap between these two forms, but the bronchioloalveolar carcinoma has sufficiently distinctive gross, microscopic and epidemiologic features.

This is a larger squamous cell carcinoma in which a portion of the tumor demonstrates central cavitation, probably because the tumor outgrew its blood supply. Squamous cell carcinomas are one of the more common primary malignancies of lung and are most often seen in smokers.

MORPHOLOGY TUMORS OF THE LUNG Adenocarcinoma

- Adenocarcinoma is the most common type of lung cancer in women and nonsmokers. The lesions are usually more peripherally located, tend to be smaller, and vary histologically from well-differentiated tumors with obvious glandular elements to papillary lesions resembling other papillary carcinomas, to solid masses with only occasional mucin-producing glands and cells. About 80 % contain mucin.
- Adenocarcinomas grow more slowly than squamous cell carcinomas.
- Peripheral adenocarcinomas are sometimes associated with areas of scarring.
- Adenocarcinomas, including bronchioloalveolar carcinomas, are less frequently associated with a history of smoking than are squamous or small cell carcinomas.

MORPHOLOGY TUMORS OF THE LUNG Adenocarcinoma

- Small Cell Carcinoma. This highly malignant tumor has a distinctive cell type. The epithelial cells are generally small, have little cytoplasm and are round or oval and, occasionally, lymphocyte-like (although they are about twice the size of a lymphocyte). This is the classic "oat cell". Other small cell carcinomas have spindle-shaped or polygonal cells and may be thus classified (spindle or polygonal small cell carcinoma). The cells grow in clusters that exhibit neither glandular nor squamous organization.

Carcinoma in situ

carcinoma which

- does not penetrate through basal membrane and
 - does not invade tissue depth is marked out separately.
- When the entire epithelium is dysplastic and no normal epithelial cells are left, then the process is beyond dysplasia and is now neoplasia. If the basement membrane is still intact, as shown here, then the process is called "carcinoma in situ" because the carcinoma is still confined to the epithelium.

■GASTRIC TUMORS

GASTRIC POLYPS

- The term "polyp" is applied to any nodule or mass that projects above the level of the surrounding mucosa. Occasionally, a lipoma or leiomyoma arising in the wall of the stomach may protrude beneath the mucosa to produce an apparent polypoid lesion. The use of the term "polyp" in the gastrointestinal tract, however, is generally restricted to mass lesions arising in the mucosa. Gastric polyps are uncommon and are found in about 0.4 % of adult autopsies and 3 to 5 % of Japanese adults. Although gastric polyps are usually found incidentally, dyspepsia or anemia resulting from blood loss may prompt the search for a gastrointestinal lesion.

GASTRIC TUMORS

- The adenoma of the stomach is a true neoplasm, representing 5 to 10 % of the polypoid lesions in the stomach. By definition, an adenoma contains proliferative dysplastic epithelium and thereby has malignant potential.

■ Adenomatous polyps are much more common in the colon. Gastric adenomas may be sessile (without a stalk) or pedunculated (stalked). The most common location is the distal portion of the stomach, particularly the antrum. These lesions are usually single and may grow up to 3 to 4 cm in size before detection. In contrast to the colon, adenomatous change may carpet a large region of flat gastric mucosa without forming a mass lesion.

GASTRIC TUMORS

■ Among the malignant tumors that occur in the stomach, carcinoma is overwhelmingly the most important and the most common (90 to 95 %). Next in order of frequency are lymphomas (4 %), carcinoids (3 %), and malignant spindle cell tumors (2 %).

■ **MORPHOLOGY.** The location of gastric carcinomas within the stomach is as follows: pylorus and antrum, 50 to 60 %; cardia, 25 %; and the remainder in the body and fundus. The lesser curvature is involved in about 40 % and the greater curvature in 22 %. Thus a favored location is the lesser curvature of the antropyloric region. Although less frequent, an ulcerative lesion on the greater curvature is more likely to be malignant.

GASTRIC TUMORS

■ Gastric carcinoma is classified basing on: 1) depth of invasion, 2) macroscopic growth pattern, and 3) histologic subtype. The morphologic feature having the greatest impact on clinical outcome is the depth of invasion. Early gastric carcinoma is defined as a lesion confined to the mucosa and submucosa, regardless of the presence or absence of perigastric lymph node metastases. Advanced gastric carcinoma is a neoplasm that has extended below the submucosa into the muscular wall and has perhaps spread more widely. All cancers presumably begin as "early" lesions, which precede the development of "advanced" lesions.

GASTRIC TUMORS

■ The three macroscopic growth patterns of gastric carcinoma, which may be evident at both the early and the advanced stages, are

- 1) exophytic, with protrusion of a tumor mass into the lumen,
- 2) flat or depressed, in which no tumor mass is visibly obvious, and
- 3) excavated, when a shallow or deeply erosive crater is present.

Adenocarcinoma

■ Carcinoma from glandular epithelium is called glandular neoplasm or adenocarcinoma.

■ It occurs in organ with corresponding epithelium and also could be of three stages of differentiation

■ (*-high differentiated, - moderate differentiated and - poorly differentiated*).

BREAST TUMORS

■ A great variety of tumors may occur in the female breast. Only the more common tumors specialized to the breast will be discussed.

■ The most common benign tumor of the female breast is fibrosarcoma - a new growth composed of both fibrous and glandular tissue. Occurring at any age within the reproductive period of life, it is somewhat more common by the age of 30.

■ Multiple small areas closely resembling a fibroadenoma are sometimes found in cases of cystic disease, termed fibroadenomatosis.

MORPHOLOGY of BREAST TUMORS

■ The fibroadenoma grows as a spherical nodule that is usually sharply circumscribed and freely movable from surrounding breast tissue. They vary in size from under 1 cm to giant forms 10 to 15 cm in diameter.

■ The histologic pattern is essentially one of delicate, cellular, fibroblastic stroma resembling intralobular stroma, enclosing glandular and cystic spaces lined by epithelium. Intact, round-to-oval gland spaces may be present, lined by single or multiple layers of cells. In other areas the connective tissue stroma appears to have undergone more active proliferation with compression of the gland spaces.

CARCINOMA of breast

■ Breast cancer causes some 20 % of cancer deaths among females and has been called the "foremost cancer" in women.

■The incidence has been increasing steadily over the past 80 years so that currently one of every nine women in the U.S. will develop cancer in their lifetime.

Classification and distribution CARCINOMA of breast

■. Among breast carcinomas small enough for their general areas of origin to be identified approximately 50 % arise in the upper quadrant; 10 % in each of remaining quadrants; and about 20 % in the central or subareolar region. The WHO classification of this tumor is as follows:

■A) Noninvasive (intraductal carcinoma, intraductal carcinoma with Paget's disease; lobular carcinoma in situ);

■B) Invasive (infiltrating) - invasive ductal carcinoma;

■invasive ductal carcinoma with Paget's disease;

■invasive lobular carcinoma;

■tubular carcinoma;

■adenoid cystic carcinoma;

■apocrine carcinoma;

■invasive papillary carcinoma.

■Only the more common types will be discussed.

CARCINOMA of breast

■Noninvasive (in situ) carcinoma - intraductal carcinoma is defined as a malignant population of cells that lack the capacity to invade through the basement membrane and therefore are incapable of distant metastasis. But these cells can spread throughout a ductal system and produce extensive lesions involving an entire sector of a breast. Movement of these cells up the main duct and into the nipple skin results in the clinical appearance of Paget's disease of the nipple.

CARCINOMA of breast

■Paget's disease is a form of ductal carcinoma, that arises in the main excretory ducts of the breast and extends intraepithelially to involve the skin of the nipple and areola. The skin lesions are invariably associated with an underlying ductal carcinoma in situ, or less common by invasive ductal carcinoma, arising deeper within the breast. The histologic hallmark of this entity is the involvement of the epidermis by malignant cells. That's why the skin of the nipple and areola is frequently fissured, ulcerated and oozing with surrounding inflammatory hyperemia and edema. The prognosis is dependent on the underlying carcinoma.

■There are some types of invasive (infiltrating) carcinoma of the breast: invasive ductal carcinoma, medullary carcinoma, colloid or mucinous carcinoma, invasive lobular carcinoma.

Large intestine carcinoma

■Wall of large intestine, deformed in favour of bank – like thickening, which considerably narrows clearance of intestine Bulge of

■ mucus tunic.

Gastric carcinomatosis.

■Multiple nodes of white color and various size are seen on gastric serous tunic.

Pancreas cancer.

■Organ is represented with white color nodes which are interunitated .

This adenocarcinoma of the pancreas is very extensive, sparing only the uncinate process at the lower left center. Chronic biliary tract obstruction from this mass produced icterus, marked by the green color of the liver after formalin fixation. Tumor invades into the hilum of liver, and small metastases to liver are also present.

At high magnification, this adenocarcinoma of the gallbladder is composed of columnar cells forming glandular and papillary structures. The prognosis with adenocarcinoma of the gallbladder is usually poor, because they have often invaded and metastasized by the time they are discovered.

The medium power microscopic appearance of an adenocarcinoma of the pancreas is seen. Just to the left of center can be seen perineural invasion by the neoplasm, which is composed of very irregular glands.

At high magnification, the microscopic appearance of an adenocarcinoma of the pancreas is seen. At the left can be seen normal pancreatic acini, but the neoplasm is composed of small irregular glands.

Poorly differentiated adenocarcinoma

- Peculiar for of *poorly differentiated adenocarcinoma* is **scirrhous carcinoma**, containing big quantity of fibrous stroma squeezing tumor parenchyma.
- Undifferentiated forms of epithelial malignant growths are represented with **small cell carcinoma**,
- Carcinoma, signet **ring cell carcinoma** and
- **medullary carcinoma**.

At high magnification, this adenocarcinoma of the pancreas has very poorly differentiated glands and extensive desmoplasia (production of collagenous stroma).

An islet cell tumor of the pancreas is seen at medium power. Note the similarity of the cells forming the neoplasm with the cells in the normal islets of the pancreas at the right.

Malignant organ-specific epithelial growths

- include chorioncarcinoma and trophoblastic tumor,
- clear-cell carcinoma of kidney, etc.
-

Renal cell carcinoma (hypernephroma).

- Tumor node is in kidney upper pole. It is striped on section, yellowish color portions alternate with portions of hemorrhages.

Features of childhood neoplasia. Dysontogenetic tumors. Teratomas and teratoblastomas **Tumors in infants.**

Peculiarities:

- they often develop from embryonal tissues as the result of their development and formation disorder – these are *dysembryomas* or *teratoid tumors (teratomas)*;
- - benign tumors (angiomas, nevi) occurs more often than malignant,
- - certain benign tumors are inclined to infiltrative growth – angiomas.
- - sarcomas (lymphosarcomas, osteosarcomas) are found more often than cancers which occur mostly in internal organs, endocrine glands;
- - malignant tumors (embryonal carcinosarcomas, hepatoma) in infants keep expansive growth for quite a long time,
- don't metastasize for long and even are able to reverse – to transfer into benign tumor – neuroblastoma into ganglioneuroma;
- - malignant tumors in infants most often are found in children of 3-5 years, which confirms significance of antenatal cancerigenic influences;

Tumors in infants.

- **Classification:** - the first type are dysembryomas, teratoid tumors or teratomas.
- They could be histoid,
- organoid,
- organizmoid and
- embryonal,
- which could be homologous – teratomas and
- heterologous – teratoblastomas.
- Histoid teratomas are also called hamartomas (angiomas, nevi, embryonal tumors of internal organs) or hamartoblastomas;

Tumors in infants

- **Classification**

■- the *second type* are tumors with embryonal cambial tissues in nervous tissue, sympathetic ganglia, adrenal glands (medulloblastomas, retinoblastomas, neuroblastomas). They are also could be referred to as hamartoblastomas,

■- the *third type* are tumors developing like adults' tumors - these are tumors of mesenchymal origin: haemoblastomas, osteogenetic and tumors of soft tissues.

Dysembryomas:

■- *hamartomas and hamartoblastomas of vascular origin*, among which

■*capillary and cavernous hemangiomas on skin* (in the form of red-bluish node) are found most often as well as in **liver** and other organs.

■ Capillary hemangiomas have ability for infiltrative growth, so they can recur after oncotomy.

■Angiosarcomas and lymphangiomas are found rarely, they can reach big size on the neck with endothelium and capillaries proliferation and infiltrative growth;

Dysembryomas:

■- *hamartomas and hamartoblastomas of cross-striated muscles – rhabdomyomas*, which are found in heart, extremes' muscles as a 10-15 cm node of grey-brown color, *rhabdomyoblastomas or embrional rhabdomyosarcoma* – malignant tumor which is found in small pelvis organs;

Dysembryomas:

■ ***hamartomas of internal organs:***

■Wilms tumor or embryonal carcinosarcoma (Wilms tumor, adenosarcoma) grow expansively in capsule for long, can reach giant size, reddish-white color with hemorrhages. Histologically in tumor among kidney tissue structures elements of mesenchymal origin are found;

■ hepato blastoma or embryonal hepatoma – malignant tumor of hepar, on section it looks like numerous white-yellowish nodes of solid fields of embryonal hepatic tissue and structures of mesenchymal origin. Metastasize, complicates with internal hemorrhages

embryonal carcinosarcoma of kidney

■ grow expansively in capsule for long,

■can reach giant size, reddish-white color with hemorrhages.

Teratomas and teratoblastomas

■organismoid and organoid teratomas – tumors derivated from three germ layers are found in *testis, ovaries, mediastinal, extraperitoneal, base of brain*.

■In girls' ovaries malignant teratoblastomas develop more often and benign teratomas – in testis, throat teratomas grow as polyps, are of benign course,

■intracranial teratomas more often are of malignant course, they often are hormonally active.

Tumors of cambial embryonal tissues:

■ medulloblastoma is malignant tumor in tentorium,

■ retinoblastoma is malignant tumor from embryonal poorly differentiated cells of retina,

■ neuroblastoma is malignant tumor in sympathetic ganglia, adrenal meddula, fast metastasizes, discharge catecholamine.

Tumors developing like adults' tumors

■are tumors of *nervous system*: astrocytomas,

■*hematopoietic system*: leucosis, malignant lymphomas;

■*bones' tumors*: osteomas, chondromas, osteosarcomas, Ewing's sarcomas.

malignant lymphomas of mediastinum

thanks