

Sarcoma - Adult Soft Tissue Cancer

What Is Cancer?

Cancer is a group of many related diseases. All forms of cancer involve out-of-control growth and spread of abnormal cells.

Normal body cells grow, divide, and die in an orderly fashion. During the early years of a person's life, normal cells divide more rapidly until the person becomes an adult. After that, normal cells of most tissues divide only to replace worn-out or dying cells and to repair injuries.

Cancer cells, however, continue to grow and divide, and can spread to other parts of the body. These cells accumulate and form *tumors* (lumps) that may compress, invade, and destroy normal tissue. If cells break away from such a tumor, they can travel through the bloodstream, or the lymph system to other areas of the body. There, they may settle and form "colony" tumors. In their new location, the cancer cells continue growing. The spread of a tumor to a new site is called *metastasis*. When cancer spreads, though, it is still named after the part of the body where it started. For example, if prostate cancer spreads to the bones, it is still prostate cancer, and if breast cancer spreads to the lungs it is still called breast cancer.

Leukemia, a form of cancer, does not usually form a tumor. Instead, these cancer cells involve the blood and blood-forming organs (bone marrow, lymphatic system, and spleen), and circulate through other tissues where they can accumulate.

It is important to realize that not all tumors are cancerous. Benign (noncancerous) tumors do not metastasize and, with very rare exceptions, are not life-threatening.

Cancer is classified by the part of the body in which it began, and by its appearance under a microscope. Different types of cancer vary in their rates of growth, patterns of spread, and responses to different types of treatment. That's why people with cancer need treatment that is aimed at their specific form of the disease.

In America, half of all men and one-third of all women will develop cancer during their lifetimes. Today, millions of people are living with cancer or have been cured of the disease. The risk of developing most types of cancer can be reduced by changes in a person's lifestyle, for example, by quitting smoking or eating a better diet. The sooner a cancer is found, and the sooner treatment begins, the better a patient's chances are of a cure.

What Is A Soft Tissue Sarcoma?

Soft tissue sarcomas are *malignant* (cancerous) tumors that can develop from fat, muscle, nerve, joint, blood vessel, or deep skin tissues. They can develop in any part of the body. Half of them develop in the arms or legs. The rest arise in the trunk, head and neck area, internal organs, or the *retroperitoneum* (the back of the abdominal cavity).

There are many types of soft tissue tumors, and not all of them are cancerous. When a tumor is not cancerous, it is called *benign*. Understanding some of the key words used to describe various types of soft tissue tumors is important.

Be aware that the term "sarcoma" in the name of a disease means the tumor is malignant. Here is a list of common tumor types that can develop from different soft tissues:

Tumors of Fat Tissue

Lipomas are benign tumors of fat tissue. They are the most common benign soft tissue tumor. Most are found under the skin, but they can develop anywhere in the body.

Lipoblastomas and *hibernomas*, like lipomas, are also benign fat tissue tumors.

Liposarcomas are malignant tumors of fat tissue. They can develop anywhere in the body, but they most often grow in the retroperitoneum.

Tumors of Muscle Tissue

Leiomyomas are benign tumors of the involuntary muscle (also called smooth muscle). This is the kind of muscle found in internal organs, such as the uterus, stomach, bowels, and blood vessels. The muscle causes these organs to contract. The most common of these is the "fibroid" tumor that many women get. It is really a leiomyoma of the *uterus* (womb).

Leiomyosarcomas are malignant tumors of involuntary muscle tissue. They can grow almost anywhere in the body, but are most often found in the retroperitoneum and the internal organs where leiomyomas also arise. Less often, they develop in the deep soft tissues of the legs or arms.

Rhabdomyomas are benign tumors of skeletal muscle (the muscle that is attached to bone and which helps us move).

Rhabdomyosarcomas are malignant tumors of skeletal muscle. These tumors most commonly grow in the arms or legs, but can also begin in the head and neck area, and in reproductive and urinary organs such as the vagina or bladder. Children are affected much more often than adults. For more information, refer to the American Cancer Society document on childhood rhabdomyosarcoma.

Tumors of Nerve Tissue

Neurofibromas, *Schwannomas*, and *neuromas* are all benign tumors of nerves.

Malignant peripheral nerve sheath tumors are malignant tumors of the cells that surround a nerve. They are also called malignant Schwannomas, neurofibrosarcomas, or neurogenic sarcomas.

Ewing's tumors are a group of related cancers that include Ewing's sarcoma of bone, *extrasketal* (not bone), Ewing's sarcoma, and *primitive neuroectodermal tumor* (PNET). All of these cancers share some features with nerve tissue of a developing embryo. They are common in children but very rare in adults. For more information, refer to the American Cancer Society document on Ewing's tumors.

Tumors of Joint Tissue

Nodular tenosynovitis is a benign tumor of joint tissue. It is most common in the hands and is more common in women than in men.

Synovial sarcoma is a malignant tumor of the tissue around joints. It tends to occur in young adults. The most common location is the knee.

Tumors of Blood Vessels or Lymph Vessels

Hemangiomas are benign tumors of blood vessels. They are rather common and are often present at birth, and can affect the skin or internal organs. They sometimes disappear without treatment.

Lymphangiomas are benign lymph vessel tumors that are usually present at birth. Lymph is a type of fluid that circulates in every tissue of the body, ending up in the venous system. It contains waste products from tissues and immune system cells.

Angiosarcomas are malignant tumors that can develop either from blood vessels (*hemangiosarcomas*) or from lymph vessels (*lymphangiosarcomas*). These tumors can sometimes develop in a part of the body that has been exposed to radiation.

Kaposi's sarcoma is a cancer formed by cells similar to those lining blood or lymph vessels. It is most common in people with the *acquired immunodeficiency syndrome (AIDS)*, but it can also develop in recipients of transplanted organs taking medication to suppress their immune system. Rarely, this cancer develops in older people with no apparent immune system problems. This disease is discussed in a separate American Cancer Society document on Kaposi's sarcoma and other HIV-related cancers.

Hemangioendothelioma is a blood vessel tumor that is less aggressive than hemangiosarcoma but still considered a low-grade cancer. It usually invades into nearby tissues and occasionally can metastasize. It may develop in soft tissues or in internal organs, such as the liver or lungs.

Tumors of fibrous and fibrohistiocytic tissue

Fibrous tissue forms tendons and ligaments. Fibrohistiocytic cells have some features of fibroblasts (fibrous tissue cells) but also have some features of histiocytes. The latter are immune system cells that surround and "digest" infectious microbes such as bacteria. *Fibromas*, *elastofibromas*, *superficial fibromatosis*, and *fibrous histiocyctomas* are all benign tumors. It is

important not to confuse the latter with *malignant fibrous histiocyoma (MFH)*, which is a malignant tumor (see below).

Fibrosarcoma is cancer of fibrous tissue. It usually affects the legs, arms or trunk.

Desmoid tumor, also called *aggressive fibromatosis*, is a fibrous tissue tumor with features in between fibrosarcoma and benign tumors such as fibromas and superficial fibromatosis. Desmoids do not metastasize, but they can invade nearby tissues and are sometimes fatal. Some doctors consider desmoids to be a type of low-grade fibrosarcoma; others believe they are a unique category of fibrous tissue tumors. Growth of some desmoid tumors is increased by certain hormones, particularly estrogen. Antiestrogen drugs are sometimes useful in treating desmoids that cannot be completely removed by surgery.

Dermatofibrosarcoma protuberans (DFSP) is a low-grade cancer of the fibrous tissue beneath the skin, usually in the trunk or limbs. It invades nearby tissues but very rarely metastasizes.

Malignant fibrous histiocyoma (MFH) is the most common malignant soft tissue tumor found in the arms or legs. Less often, it can develop in the retroperitoneum. This sarcoma is most common in older adults.

Tumor of Perivascular Tissue

Perivascular means "around vessels." Normal perivascular cells help control the amount of blood flowing through blood vessels.

Glomus tumors are benign perivascular tumors. They usually are found under the skin of the fingers.

Hemangiopericytoma is a sarcoma of perivascular tissue. It most often develops in the legs, pelvis, and retroperitoneum.

Tumors of Uncertain Tissue Type

Microscopic examination and other laboratory tests can usually find similarities between most sarcomas and certain types of normal soft tissues. However, some sarcomas have no apparent origin from a specific type of normal soft tissue.

Myxoma is a benign tumor that usually is located in muscles but does not develop from muscle cells. The cells of a myxoma produce mucus-like material, which is the most characteristic feature of this tumor.

Malignant *mesenchymoma* is a rare type of sarcoma that contains some areas showing features of fibrosarcoma and other areas with features of at least two other types of sarcoma.

Alveolar soft-part sarcoma is a rare cancer predominantly affecting young adults. The legs are the most common location of these tumors.

Epithelioid sarcoma most often develops in tissues under the skin of the hands, forearms, feet, or lower legs. Adolescents and young adults are often affected.

Clear cell sarcoma is a rare cancer that often develops in tendons and related tissues. Under the microscope, it shares some features with malignant melanoma, a type of cancer that develops from pigment-producing skin cells. How cancers with these features develop in parts of the body far from the skin is not known.

Desmoplastic small cell tumor is a rare sarcoma of adolescents and young adults, found most often in the abdomen. Its name means that it is formed by small round cancer cells surrounded by scar-like tissue.

Tumor-like Conditions of Soft Tissue

Some conditions of soft tissues are caused by inflammation or injury and can form a mass that looks like a soft tissue tumor. Unlike a true tumor, they do not originate from a single abnormal cell, have limited capacity to grow or spread to nearby tissues, and never spread through the bloodstream or lymph system. Examples include *nodular fasciitis* and *myositis ossificans*, which involve tissues under the skin and muscle tissues, respectively.

What Are The Key Statistics About Soft Tissue Sarcomas?

The American Cancer Society estimates that in 2001 approximately 8,700 new soft tissue sarcomas will be diagnosed in the United States. Of these, 4,600 cases will be diagnosed in males, while 4,100 cases will be diagnosed in females. During 2001, it is also estimated that 4,400 Americans (2,100 males and 2,300 females) will die of soft tissue sarcomas. These statistics include both adults and children.

What Are The Risk Factors For Soft Tissue Sarcomas?

A *risk factor* is anything that increases a person's chance of getting a disease such as cancer. Different cancers have different risk factors. For example, unprotected exposure to strong sunlight is a risk factor for skin cancer and smoking is a risk factor for cancers of the mouth, throat, lungs, bladder, kidneys, and several other organs. Scientists have found several risk factors that make a person more likely to develop soft tissue sarcomas.

Ionizing radiation: This risk factor accounts for only a small percentage of sarcomas (less than 5%). The most common cause of radiation exposure in patients who develop sarcomas is from radiation given to treat other tumors, such as breast cancer, or lymphoma. The average time between radiation exposure and diagnosis of a sarcoma is about 10 years. Radiation therapy techniques have steadily improved over several decades. Treatments now target the cancers more precisely, and more is known about selecting radiation doses. These advances are expected to reduce the number of secondary cancers resulting from radiation therapy. However, it is

important to realize that oncologists prescribe radiation therapy only when its benefits (improved survival rate and relief of symptoms) outweigh the risk of this and other complications.

Family history: Certain inherited conditions increase a person's risk of developing soft tissue sarcomas.

Neurofibromatosis is a disease that usually runs in families and is characterized by many *neurofibromas* (benign tumors that form in nerves under the skin and in other parts of the body). One or more neurofibromas will develop into a malignant peripheral nerve sheath tumor in about 5% of people with neurofibromatosis.

Gardner's syndrome, a disease that runs in families and leads to benign *polyps* (precancerous growths) and cancers in the intestines, also causes desmoid tumors (a type of low-grade fibrosarcoma) in the abdomen and benign bone tumors.

Li-Fraumeni syndrome runs in families and increases the risk of developing breast cancer, brain tumors, leukemias, and cancer of the adrenal glands.. People with Li-Fraumeni syndrome also have an increased risk of developing soft tissue sarcomas and bone sarcomas. If their cancer is treated with radiation, they have a very high chance of developing a new cancer in the part of the body that received the radiation.

Retinoblastoma (an eye cancer of children) can be caused by an inherited predisposition. Children with the inherited form of retinoblastoma also have an increased risk of developing bone or soft tissue sarcomas.

Damaged lymph nodes: Lymph (a clear fluid containing immune system cells) is transported throughout the body by lymph vessels and filtered by lymph nodes (bean-sized collections of immune system cells). Lymphangiosarcomas, a cancer of lymph vessels, can develop in parts of the body where lymph nodes have been removed surgically or damaged by radiation therapy. Although this is a rare complication, it affects some women whose axillary lymph nodes were removed and irradiated to treat their breast cancer.

Chemicals: Vinyl chloride (a chemical used in making plastics) exposure is a risk for developing sarcomas of the liver, but it has not been proven to cause soft tissue sarcomas. Exposure to dioxin and to herbicides that contain phenoxyacetic acid at high doses (for example, farm workers who work closely with these chemicals) may also be risk factors, but this is not known for certain. There is no evidence that herbicides (weed killers) or insecticides cause sarcomas at levels encountered by the general public.

Injury: This is not a risk factor for developing sarcomas. In the past, this issue has been a source of confusion. One reason is that injury may produce a swelling that resembles a tumor but is not a true tumor. Also, pain from an injury draws a person's attention to the injured area, making it more likely that the sarcoma will be discovered, even though it had been present for some time.

Do We Know What Causes Soft Tissue Sarcomas?

Although scientists still do not know exactly what causes most cases of soft tissue sarcoma, they have identified several risk factors that can make a person more likely to develop these cancers. And, recent research has shown that some of these risk factors affect the DNA of cells in the soft tissues.

Researchers have made great progress in understanding how certain changes in DNA can cause normal cells to become cancerous. DNA is the molecule that carries the instructions for nearly everything our cells do. We usually resemble our parents because they are the source of our DNA. However, DNA affects more than our outward appearance. Some *genes* (parts of our DNA) contain instructions for controlling when our cells grow and divide. Certain genes that promote cell division are called *oncogenes*. Others that slow down cell division or cause cells to die at the appropriate time are called *tumor suppressor genes*. It is known that cancers can be caused by DNA *mutations* (defects) that turn on oncogenes or turn off tumor suppressor genes. Several cancer family syndromes have been found in which inherited DNA mutations cause a very high risk of developing breast, colon, kidney, eye, or other cancers. In some of these, there is also an increased risk of developing soft tissue sarcomas. Researchers have characterized many of these DNA changes in the past few years.

Four inherited conditions that increase a person's risk of developing soft tissue sarcoma were noted in the section on risk factors. All four (neurofibromatosis, Gardner's syndrome, Li-Fraumeni syndrome, and inherited retinoblastoma) are due to inheriting mutated tumor suppressor genes. Mutations of these genes can be detected by genetic testing. People with a strong family history of sarcomas or other cancers occurring at a young age may wish to discuss the benefits and disadvantages of genetic testing with their doctor. The American Cancer Society recommends that genetic testing results should always be explained by a genetic counselor or a specially trained physician who knows about the implications of these results and strategies for early cancer detection in high-risk patients.

DNA mutations causing soft tissue sarcoma are common. They are usually acquired during life rather than having been inherited before birth. Acquired mutations may result from exposure to radiation or cancer-causing chemicals. In most sarcomas, they occur for no apparent reason.

Researchers still do not know why most soft tissue sarcomas develop in people who have no apparent risk factors.

Can Soft Tissue Sarcomas Be Prevented?

The only way to prevent some soft tissue sarcomas is to avoid exposure to risk factors whenever this is possible. However, since most sarcomas develop in people with no known risk factors, there is no way known at this time to prevent most cases.

Can Soft Tissue Sarcomas Be Found Early?

Members of families with increased risk of sarcomas due to inherited gene mutations should discuss genetic testing with their physicians. They should notify their physician promptly of any lumps or growths.

No screening tests and examinations are recommended for people who have no family history of sarcoma or other sarcoma risk factors. For these people, the best approach to early detection is to notify their health care professional of any unexplained lumps or growths, or other symptoms that may be caused by a soft tissue sarcoma.

Signs and Symptoms of Soft Tissue Sarcomas

When sarcomas develop on the arms or legs, most people simply notice a new mass which has grown over a period of time (weeks to months). Generally, the mass doesn't hurt; about one-third of the time the mass is painful.

When sarcomas grow in the abdomen, the symptoms they cause aren't very specific. About 1/3 of the time they can cause pain. Sometimes they are found because they cause blockage or bleeding of the stomach or bowels. They can also be found because they have grown large enough to be felt in the abdomen.

If you have any of the following problems, see a doctor right away:

- A new lump or a lump which is growing anywhere on your body.

- Severe or worsening abdominal pain.

- Blood in your stool or vomit (when bleeding happens in the stomach or bowels, the blood isn't always red, and it may make the stool look very black and tarry).

Since symptoms of soft tissue sarcomas often do not appear until the disease is advanced, only about 50% of soft tissue sarcomas are found in the early stages, before they have spread. The 5-year survival rate for people with soft tissue sarcomas is around 90% if the cancer is found while it is small and before it has spread. In contrast, the 5-year survival rate is between 10% and 15% for sarcomas that have *metastasized* (spread).

The 5-year survival rate refers to the percent of people who live at least 5 years after their cancer is diagnosed. Many of these patients live much longer than 5 years after diagnosis, and 5-year rates are used to produce a standard way of discussing prognosis. Five-year *relative* survival rates exclude from the calculations patients dying of other diseases, and are considered to be a more accurate way to describe the prognosis for people with a particular type and stage of cancer. Of course, 5-year survival rates are based on patients diagnosed and initially treated more than 5 years ago. Improvements in treatment often result in a more favorable outlook for recently diagnosed patients.

How Are Soft Tissue Sarcomas Diagnosed?

If there are symptoms or other reasons that suggest you may have a sarcoma, the doctor will use one or more methods to find out if the disease is really present.

Medical History and Physical Exam

A complete medical history is a health interview to check for risk factors and symptoms. A physical exam to provide other information about signs of sarcomas and other health problems.

Imaging Tests

Ultrasound: This test uses sound waves (like sonar). The pattern of echoes produced when the sound wave is reflected off normal tissues and tumors are different, allowing a mass to be identified.

Computed tomography (CT scan): This is an x-ray procedure in which the x-ray beam moves around the body, taking pictures from different angles. These images are combined by a computer to produce a detailed cross-sectional picture of the inside of the body.

Magnetic resonance imaging (MRI): This procedure uses large magnets and radio waves to produce computer-generated cross-sectional pictures of internal organs. The pictures look very similar to a CT scan, but offer some advantages. For example, MRI scans show blood vessels in greater detail and allow the cross-sectional views to be shown from different directions.

Biopsy

A *biopsy* removes a sample of tissue from the tumor for examination using the microscope and in some cases, by other laboratory tests. Although a physical exam and imaging tests may suggest that a mass is likely to be a sarcoma, a biopsy is the only way to be certain it is a sarcoma and not another type of cancer or a noncancerous disease.

If a sarcoma is present, the biopsy will determine what type it is (for example, leiomyosarcoma, liposarcoma, or fibrosarcoma) and its *grade*. The grade of a sarcoma is based on the cancer's appearance under the microscope. It provides a rough estimate of how rapidly it will grow and spread.

The *grading system* used most often divides sarcoma into three categories low-grade or grade 1, intermediate-grade or grade 2, and high-grade or grade 3. The grade of a sarcoma is valuable in predicting a patient's outlook for survival and is one of the pieces of information used in determining it's the stage of a sarcoma (see How Are Soft Tissue Sarcomas Staged?)

There are several types of biopsies that may be used in diagnosing sarcomas. Doctors with experience in these tumors will choose one, based on the size and location of the tumor.

Fine needle aspiration (FNA) biopsy: FNA uses a very thin needle and an ordinary syringe to withdraw small fragments of tissue from the tumor mass. The doctor can aim the needle while feeling a mass near the surface of the body. If the tumor is deep inside the body, the needle can be guided while it is viewed by a CT scan. The main advantage of FNA is that it does not require surgery. The disadvantage is that in many cases the thin needle cannot remove enough tissue to be certain that a sarcoma is present or to accurately determine its type or grade. FNA is often useful in showing that a mass initially thought to be a sarcoma (found on physical exam or imaging tests) is actually another type of cancer, a benign tumor, an infection, or some other disease. If FNA results suggest a sarcoma, another type of biopsy will usually follow to remove enough tissue to be certain of that diagnosis. After a sarcoma is diagnosed, FNA is most useful in determining whether additional tumors in other organs are metastases.

Core needle biopsy or Tru-cut biopsy: The needle used for this biopsy is larger than the FNA needle. It removes cylindrical pieces of tissue about 1/16 inch across. In most cases, it removes enough tissue to see whether a sarcoma is present.

Excisional or incisional biopsy: A surgeon cuts through the skin to remove the entire mass (*excisional biopsy*) or a small part of a large tumor (*incisional biopsy*). This method almost always provides enough tissue to make a diagnosis of the exact type and grade of sarcoma and is the most certain approach. If the tumor is near the skin surface, this is a simple operation that can be done with *local or regional anesthesia* (numbing medication given near the mass or into a nerve). But if the tumor is deep inside the body, *general anesthesia* is used (the patient is asleep). If a tumor is relatively small, near the surface of the body, and not located near critical tissues (such as important nerves or large blood vessels), an excisional biopsy is often used to remove the entire mass and a margin of normal tissue. This combines the diagnostic biopsy and surgical treatment into one operation.

Proper biopsy technique is a very important part of successful treatment of soft tissue sarcomas. An incisional biopsy of a soft tissue mass should be performed by a surgeon experienced in sarcoma treatment. The incision should be planned so that the wound resulting from the biopsy can be completely removed later on as part of a wide excision (if the mass is found to be a sarcoma). An incisional biopsy in the wrong place or an excision without wide enough margins can make it harder to completely remove a sarcoma without causing too much damage to that part of the body.

Special testing of biopsy samples: Sometimes, special tests may also be needed in some cases to accurately determine whether a sarcoma is present and, if so, what type.

Immunohistochemistry involves treating a part of the biopsy sample with special laboratory antibodies that recognize cell proteins typical of certain kinds of sarcomas. The cells are treated with additional chemicals that cause the cells containing the specific proteins to change color. The color change is then detected under a microscope.

Cytogenetics examines cells with a microscope to see if part of one chromosome is abnormally attached to part of a different chromosome as happens in certain types of sarcomas. To clearly view the chromosomes, it is usually necessary for the malignant cells to be grown in laboratory flasks for at least a week. A new method, called *fluorescent in situ hybridization (FISH)* can

sometimes be used to detect chromosome changes without first growing the cells in the lab. Although tests of chromosome changes are not necessary for diagnosis of most sarcomas, they are sometimes very useful. And, as new changes are discovered, these tests may become more important and more common.

How Are Soft Tissue Sarcomas Staged?

The staging process collects and summarizes information about how large the sarcoma is and whether it has spread. The stage of a sarcoma is the most significant factor in determining each patient's prognosis (the outlook for chances of survival), and in selecting treatment options.

Collecting the information needed for staging involves biopsies, imaging tests of the main tumor (usually with CT or MRI scans) and imaging tests of other parts of the body the cancer may have spread to.

A staging system is a standard way for the cancer care team to summarize the extent of a cancer's spread. The staging system used often to stage sarcomas is the TNM system of American Joint Committee on Cancer. **T** stands for the size of the tumor, **N** stands for spread to lymph nodes (bean-sized collections of immune system cells found throughout the body that help fight infections and cancers), and **M** is for metastasis (spread to distant organs). In soft tissue sarcomas, an additional factor, called histologic grade or **G**, is used to stage the tumor. The histologic grade is based on how the sarcoma cells appear under the microscope. To assign a stage, information about the tumor, its grade, lymph nodes, and metastasis is combined by a process called *stage grouping*. The stage is described by Roman numerals from I to IV with the letters A or B.

Histologic Grade

G1: low grade (the least aggressive appearing under the microscope)
G2: moderate grade (intermediate between G1 and G3)
G3: high grade (the most aggressive appearing under the microscope)

Tumor

T1: the sarcoma is less than 5 centimeters (2 inches)
T2: the sarcoma is 5 centimeters or greater in size

Lymph Nodes

N0: no lymph nodes have sarcoma cells in them
N1: lymph nodes are present which have sarcoma cells in them

Metastasis

M0: no distant metastases (spread) of sarcoma are found
M1: distant metastases of sarcoma are found

Stage Grouping for Soft Tissue Sarcomas

Stage IA G1,T1,N0,M0

Stage IB G1,T2,N0,M0

Stage IIA: G2,T1,N0,M0

Stage IIB: G2,T2,N0,M0

Stage IIIA: G3,T1,N0,M0

Stage IIIB: G3,T2,N0,M0

Stage IVA: Any G, Any T,N1,M0

Stage IVB: Any G, Any T, Any N, M1

As examples of stage grouping, a grade 2 sarcoma that is 3 inches across, without any metastases is Stage 2B, but if the sarcoma had spread to the lungs it would be Stage IVB.

This staging system is very useful in estimating prognosis and selecting treatment, but, additional factors, such as sarcoma location, are also considered when selecting treatment.

How Are Soft Tissue Sarcomas Treated?

After a sarcoma is found and staged, the cancer care team will recommend one or several treatment options to consider. This is an important decision, so it is important to take time and think about all of the choices. In choosing a treatment plan, factors to consider include the type, location and stage of the cancer, as well as the patient's overall physical health.

It is often a good idea to seek a second opinion. A second opinion can provide more information and help the patient feel more confident about the treatment plan that is chosen.

Surgery for Soft Tissue Sarcomas

Depending on the type and stage of a sarcoma, surgery may be used to remove the cancer and some of the surrounding tissue. The goal of surgery is to remove the tumor and at least 2-3 centimeters (about 1 inch) of the tissue surrounding the tumor. When the tumor is in the abdomen, this amount of surgery is more difficult because the tumor may be next to vital organs that can't be surgically removed.

In the past, about half of all sarcomas in an arm or leg, were treated by amputating the limb. Amputations are rarely done now (about 5% of the time) because we know that patients treated with limb-sparing surgery followed by *adjuvant* (additional) radiation therapy have the same overall survival rates as those who have amputations. Currently, amputations are recommended only for very specific situations. For example, when essential nerves, arteries, or muscles are surrounded by invading sarcoma cells, amputation may be the only way to remove all of the cancer. Sometimes, removing critical nerves, muscles and blood vessels together with the cancer

would leave a limb unable to function usefully or one that is chronically painful, and then amputation may be the best option. If distant metastases to the lungs or other organs are found and complete surgical removal of all cancer (all metastases as well as the original tumor) is not considered possible, then amputation is not recommended. Occasionally, chemotherapy and radiation given prior to surgery may facilitate surgical resection. This strategy is also used for high grade sarcomas of high risk for developing metastases because it may provide an indication of tumor response and allow early initiation of treatment for presumed (micro) metastases.

Most of the time when a sarcoma has metastasized, surgical therapy cannot cure the cancer. However, if the only sign of metastatic sarcomas is in the lung, the metastatic tumor can sometimes be surgically removed. This type of surgery can lead to long-term survival. Studies of patients who have had surgery for metastatic soft tissue sarcomas in the lung show that between 20% and 30% of these patients are alive five years later.

Radiation Therapy for Soft Tissue Sarcomas

Radiation therapy uses high energy radiation to kill cancer cells.

External beam radiation therapy uses radiation delivered from outside the body that is focused on the cancer. This is the type of radiation therapy most often used to treat sarcomas.

Brachytherapy uses a small pellet of radioactive material placed directly into the cancer. Brachytherapy may be used as the only form of radiation therapy or in combination with external beam radiation.

Radiation therapy is sometimes used as the *primary* (main) treatment of sarcomas in some patients, especially patients whose general health is too poor to undergo surgery. After surgery, radiation as an *adjuvant* (additional) therapy can be used to kill very small clusters of cancer cells that cannot be seen and removed during surgery. Radiation therapy can also be used to palliate, or ease, symptoms of sarcomas.

Side effects of radiation therapy may include mild skin problems or fatigue. These often go away after a short while. Radiation may also make the side effects of chemotherapy worse. Abdominal radiation therapy may cause nausea and diarrhea, while radiation to the chest may cause lung damage and lead to difficulty breathing and shortness of breath. Radiation of large areas of an arm or leg can cause swelling, pain, and weakness. Side effects of radiation therapy to the brain for metastatic sarcoma usually become most serious one or two years after treatment, and include headaches and difficulty thinking.

Chemotherapy for Soft Tissue Sarcomas

Chemotherapy uses anticancer drugs that are given into a vein or taken by mouth. These drugs enter the bloodstream and reach all areas of the body, making this treatment useful for cancer that has spread or metastasized to other organs. Depending on the type and stage of sarcoma, chemotherapy may be given as the *primary* (main) treatment or as an *adjuvant* (addition) to

surgery. Chemotherapy for soft tissue sarcoma generally uses a combination of several anticancer drugs.

The most commonly used drugs are ifosfamide and doxorubicin. Sometimes other drugs such as dacarbazine, methotrexate, vincristine, cisplatin, paclitaxel, and others are added in combination. When several drugs are used together, the combination is given a shortened name such as: MAID (combined Mesna, doxorubicin (Adriamycin), ifosfamide, and dacarbazine) or AIM (doxorubicin, ifosfamide and Mesna). Mesna is a drug used to protect the bladder from the severe irritation often caused by ifosfamide.

Chemotherapy drugs kill cancer cells but also damage some normal cells. Therefore, careful attention must be given to avoiding or minimizing side effects, which depend on the type of drugs, the amount taken, and the length of treatment. Temporary side effects might include nausea and vomiting, loss of appetite, loss of hair, and mouth sores. Because chemotherapy can damage the blood-producing cells of the bone marrow, patients may have low blood cell counts. This can result in an increased chance of infection (due to a shortage of white blood cells), bleeding or bruising after minor cuts or injuries (due to a shortage of blood platelets), and fatigue (due to low red blood cell counts). A particular side effect of ifosfamide is damage to the bladder. For this reason, it is generally given with Mesna, a drug that protects the bladder.

Most side effects disappear once treatment is stopped. Hair will grow back after treatment ends, though it may look different. There are remedies for many of the temporary side effects of chemotherapy. For example, *antiemetic* drugs to prevent or reduce nausea and vomiting can be given.

Some side effects may be permanent, however. Doxorubicin, in particular, can weaken the heart, so the doctor may do special studies of the heart before starting this drug or during a course of therapy with this drug. Chemotherapy may damage the ovaries or testicles, sometimes causing infertility (not being able to have children) that may be permanent.

Complementary and Alternative Methods

If you are considering any unproven alternative or complementary treatments, it is best to discuss this openly with your cancer care team and request information from the American Cancer Society or the National Cancer Institute. Some unproven treatments can interfere with standard medical treatments or may cause serious side effects.

Clinical Trials

Studies of promising new or experimental treatments in patients are known as clinical trials. A clinical trial is only done when there is some reason to believe that the treatment being studied may be of value to the patient. Treatments used in clinical trials are often found to have real benefits. There are three phases of clinical trials in which a treatment is studied before the treatment is eligible for approval by the FDA (Food and Drug Administration).

The purpose of a Phase I study is to find the best way to give a new treatment and how much of it can be given safely. Physicians watch patients carefully for any harmful side effects. The research treatment has been well tested in laboratory and animal studies, but the side effects in patients are not completely predictable.

Phase II trials determine the effectiveness of a research treatment after safety has been evaluated in a Phase I trial. Patients are closely observed for an anticancer effect by careful measurement of cancer sites present at the beginning of the trial. In addition to monitoring patients for response, any side effects are carefully recorded and assessed.

Phase III trials require entry of large numbers of patients. Some trials enroll thousands of patients. One of the groups may receive standard (the most accepted) treatment, so the new treatments can be directly compared. The group that receives the standard treatment is called the "control group." For example, one group of patients (the control group) may receive the standard chemotherapy for a certain type of cancer, while another patient group may receive a different type of chemotherapy, that may or may not contain an investigational drug, to see if this improves survival. All patients in Phase III trials are monitored closely for side effects, and treatment is discontinued if the side effects are too severe.

Researchers conduct studies of new treatments to answer the following questions:

- Is the treatment likely to be helpful?
- Does this new type of treatment work?
- Does it work better than other treatments already available?
- What side effects does the treatment cause?
- Do the benefits outweigh the risks, including side effects?
- In which patients is the treatment most likely to be helpful?

However, there are some risks. No one involved in the study knows in advance whether the treatment will work or exactly what side effects will occur. That is what the study is designed to discover. While most side effects will disappear in time, some can be permanent or even life-threatening. Keep in mind that even standard treatments have side effects. Depending on many factors, a patient may decide that a clinical trial will be beneficial.

Enrollment in any clinical trial is completely up to you. Your doctors and nurses will explain the study to you in detail and will give you a form to read and sign indicating your desire to take part. This process is known as giving your *informed consent*. Even after signing the form and after the clinical trial begins, you are free to leave the study at any time, for any reason. Taking part in the study does not prevent you from getting other medical care you may need.

To find out more about clinical trials, ask your cancer care team. Among the questions you should ask are:

- What is the purpose of the study?
- What kinds of tests and treatments does the study involve?
- What does this treatment do?

- What is likely to happen in my case with, or without, this new research treatment?
- What are my other choices and their advantages and disadvantages?
- How could the study affect my daily life?
- What side effects can I expect from the study? Can the side effects be controlled?
- Will I have to be hospitalized? If so, how often and for how long?
- Will the study cost me anything? Will any of the treatment be free?
- If I am harmed as a result of the research, what treatment would I be entitled to?
- What type of long-term follow-up care is part of the study?
- Has the treatment been used to treat other types of cancers?

You can get a list of current clinical trials by calling the National Cancer Institute's Cancer Information Service toll free at 1-800-4-CANCER or visiting the NCI clinical trials website for patients (cancertrials.nci.nih.gov) or healthcare professionals (cancernet.nci.nih.gov/prot/protsrch.shtml).

Treatment Choices by Stage of Soft Tissue Sarcomas

Stage I: Most patients with stage I sarcomas have their cancers surgically removed. When it is not possible to remove the tumor plus at least two centimeters (about 1 inch) of normal tissue around the tumor, radiation therapy is generally added after surgery. Sometimes radiation therapy is done before surgery to shrink the tumor and improve the chance for completely removing it. Radiation may be used instead of surgery if the tumor is considered unresectable (unable to be removed completely) either because it is too large, because it surrounds critical nerves or blood vessels, or because the patient has other serious health problems and cannot undergo surgery. Getting the entire tumor and enough normal tissue around the tumor is surgically more difficult when the tumor is in the head, neck, or abdomen, and so radiation is often given when the tumor is in one of those areas. Around 85%-90% of people with stage I tumors are alive five years after diagnosis.

Stage II: Surgical removal of the tumor is still the goal with stage II tumors. Ideally, surgical treatment involves removal of the tumor and several centimeters (over an inch) of normal tissue around the tumor in all directions. Because this is often not possible, radiation therapy is often given as adjuvant treatment after surgery. In rare cases, amputation is needed to completely remove the tumor. As with stage I sarcomas, radiation therapy can be used alone when the tumor's location or size or the patient's general state of health makes surgery impossible. There is evidence that chemotherapy after surgery may benefit some people with stage II sarcomas. Between 70% to 80% of people with Stage II tumors are alive five years after diagnosis.

Stage III: Treatment of stage III tumors is similar to stage II tumors. However, these tumors have a greater chance of returning. For this reason, radiation therapy is generally used before or after surgery. Also, there is some evidence that chemotherapy in addition to surgery is useful. About 60% of people with stage III tumors are alive five years after diagnosis.

Stage IV: The usual treatment for stage IVA sarcomas is surgical removal of the *primary* (main) tumor with a wide (over 1 inch) margin of normal tissue whenever possible, and surgical

removal of nearby lymph nodes, followed by radiation therapy. Radiation therapy before surgery may help with complete removal of some tumors. In others, amputation may be required.

Because stage IVB sarcomas have spread to distant organs, cure is usually not possible. However, cure is sometimes possible for patients whose main tumor and all of their metastases can be removed by surgery. Those patients' main tumors should be treated as in stages II or III, and metastases should be completely removed, if possible.

For patients whose primary tumor and all metastases cannot be completely removed by surgery, palliative radiation therapy and/or chemotherapy is recommended. Around 10%-15% of patients with stage IV tumors are alive five years after diagnosis.

What Should You Ask Your Doctor About Soft Tissue Sarcomas?

As noted earlier, it is important to have frank, open discussions with your cancer care team. They want to answer all of your questions, no matter how trivial they might seem.

For instance, consider these questions:

- What kind of sarcoma do I have?
- Has my cancer spread beyond the primary site?
- What is the stage of my cancer and what does that mean in my case?
- What treatment choices do I have?
- What do you recommend and why?
- What risks or side effects are there to the treatments you suggest?
- What are the chances of recurrence of my cancer with these treatment plans?
- What should I do to be ready for treatment?
- Based on what you've learned about my cancer, how long do you think I'll survive?

In addition to these sample questions, be sure to write down some of your own. For instance, you might want more information about recovery times so you can plan your work schedule. Or, you may want to ask about second opinions or about clinical trials for which you may qualify.

What Happens After Treatment For Soft Tissue Sarcomas?

During and after treatment for your soft tissue sarcoma, you may be able to hasten your recovery and improve your quality of life by taking an active role. Learn about the benefits and disadvantages of each of your treatment options, and ask questions of your cancer care team if there is anything you do not understand. Learn about and look out for side effects of treatment, and report these promptly to your cancer care team so that they can take steps to minimize them and shorten their duration.

Remember that your body is as unique as your personality and your fingerprints. Although understanding your cancer's stage and learning about the effectiveness of your treatment options can help predict what health problems you may face, no one can say precisely how you will respond to cancer or its treatment.

You may have special strengths such as a history of excellent nutrition and physical activity, a strong family support system, or a deep faith, and these strengths may make a difference in how you respond to cancer. In fact, behavioral scientists have recently found that some people who took advantage of a social support system, such as a cancer support group, survived with a better quality of life. There are also experienced professionals in mental health services, social work services and pastoral services who may assist you in coping with your illness.

You can also help in your own recovery from cancer by making healthy lifestyle choices. If you use tobacco, stop now. Quitting will improve your overall health and the full return of the sense of smell may help you enjoy a healthy diet during recovery. If you use alcohol, limit how much you drink. Have no more than one or two drinks per day. Good nutrition can help you get better after treatment. Eat a nutritious and balanced diet, with plenty of fruits, vegetables, and whole grain foods. Ask your cancer care team if you could benefit from a special diet -- they may have specific recommendations for people who have had abdominal radiation therapy.

If you are in treatment for cancer, be aware of the battle that is going on in your body. Radiation therapy and chemotherapy add to the fatigue caused by the disease itself. Give your body all the rest it needs so that you will feel better as time goes on. Exercise once you feel rested enough. Ask your cancer care team whether your cancer or its treatments might limit your exercise program or other activities.

Surgery and radiation therapy may sometimes affect a person's feelings about their body, and may lead to specific physical problems that affect sexuality. Your cancer care team can help with these issues, so don't hesitate to share your concerns.

A cancer diagnosis and its treatment are major life challenges, with an impact on you and everyone who cares for you. Before you get to the point where you feel overwhelmed, consider attending a meeting of a local support group. If you need individual assistance in other ways, contact your hospital's social service department or the American Cancer Society for help in contacting counselors or other services.

Follow-up tests: Frequent physical examinations are done to detect tumor recurrence or side effects of treatment as early as possible. Chest x-rays and other imaging studies (such as ultrasound, CT scans, and MRI scans) may be done to watch for recurrence or metastasis. Most local recurrences and many distant recurrences (*metastases*) can be effectively treated, particularly when they are found early. The lungs are the most common site of distant recurrence of sarcoma. Many lung recurrences can be surgically removed, often resulting in improved survival and sometimes in a cure.

New symptoms: It is important for the patient to report any new symptoms such as cough to the doctor right away, since they may indicate cancer recurrences or side effects of treatment.

What's New In Soft Tissue Sarcoma Research And Treatment?

There is always research going on in the area of soft tissue sarcomas. Scientists are learning more about causes and ways to prevent sarcomas, and doctors are working to improve treatments.

Basic Research: There has been much progress in understanding how certain changes in the DNA of soft tissue cells cause sarcomas to develop. This information is already being applied to new tests for diagnosis and classification of sarcomas. This is important, since accurate classification helps doctors in selecting the most appropriate treatment. It is hoped that this information will soon lead to new strategies for treating these cancers, based on specific differences between normal and malignant soft tissue cells.

Chemotherapy: Active research is ongoing in chemotherapy for soft tissue sarcomas. This includes studies of new drugs and new ways to give drugs now available. For example, clinical trials are now testing the value of giving chemotherapy before surgery, or of injecting chemotherapy directly into the artery that supplies blood to the arm or leg containing a sarcoma (regional chemotherapy). Recent trials have suggested new drugs which may limit the degree of heart damage which the chemotherapy drug doxorubicin (Adriamycin) can cause. This may allow using higher doses of doxorubicin, which could lead to better long-term survival rates, but follow-up heart exams will still need to be obtained routinely.

Radiation therapy: Studies of new radiation therapy methods are also in progress. For example, the roles of external beam radiation and *brachytherapy* (internal radiation) are being clarified. Use of *intraoperative* (during surgery) radiation therapy for abdominal and retroperitoneal sarcomas is being tested.

Immunotherapy: Experimental treatments that boost the patient's immune reaction to fight soft tissue sarcomas more effectively are being tested. Some treatments use drugs like interleukin-2 that boost the immune system in general. In *active immunotherapy*, the patient is given vaccines that might cause the immune system to recognize some of the abnormal chemicals in sarcomas and kill these cells. *Passive immunotherapy* uses antibodies made in the laboratory to seek out sarcoma cells that contain certain abnormal cancer cell proteins. Often, toxins or radioactive atoms are attached to these antibodies, so that the cell-killing chemicals or radiation are targeted specifically to the cancer cells and do not attack the healthy cells of the body.

National Organizations And Web Sites

The following organizations can also provide additional information and resources . *

National Cancer Institute
Telephone: 1-800-4-CANCER
Internet Address: www.nci.nih.gov

*Inclusion on this list does not imply endorsement by the American Cancer Society

Additional Resources

American Cancer Society Information

Caring for the Patient with Cancer at Home (Booklet; Code# 4656)

Murphy, Gerald P., Lois B. Morris, and Dianne Lange. *Informed Decisions: The Complete Book of Cancer Diagnosis, Treatment, and Recovery*. Viking, 1997. New York: (Book; Code #9449)

Questions and Answers About Pain Control (Booklet: Code# 4518)

Other Publications*

A Cancer Survivor's Almanac: Charting Your Journey. Edited by Barbara Hoffman, JD. National Coalition for Cancer Survivorship. Minnetonka, MN: Chronimed Publishing, 1996.

Dollinger, Malin, Ernest H. Rosenbaum, and Greg Cable. *Everyone's Guide to Cancer Therapy*. Kansas City: MO: Somerville House Books, 1994.

Morra, Marion and Eve Potts. *Choices*. New York: Avon Books, 1994.

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Revised: 03/22/2000