

A “tumor” or “suspected tumor” diagnosis is a major setback in any person’s life. Right from the start - in the initial phase of the patient’s personal confrontation with the disease, possibly characterized by fear, uncertainty and even outright despair - the situation requires intensive cooperation. The patient will probably be required to undergo a great many clinical and instrumental examinations and tests, answer questionnaires, and participate in discussions in the immediate follow-up to the suspected diagnosis “tumor,” for an exact diagnosis must be reached as quickly as possible.

The objective of all of these examinations, questions, and tests is to obtain answers to the following questions:

- Is the tumor benign or malignant (dignity)?
- Exactly what type of tumor is it?
- What is the extent of tumor spread?
- Is it the type of tumor that originates primarily in bone, or is it a metastasis (spread of tumor tissue to a new location in the body) originating from a tumor located outside the spinal column?
- Are metastases present in other organs as well (liver, lungs, lymph nodes)?
- What is the tumor’s stage of development (staging)?
- What therapies are available to treat the tumor (surgery, radiotherapy, chemotherapy)?

Not until the initial workup has answered these important questions is it possible to give the patient a reliable and consistent description of the clinical picture as a basis for a discussion of the consequences of the disease as well as possible therapeutic approaches, risks, and complications. Since tumor disease always consists of a complex clinical picture that normally concerns a number of different medical specialties, standard procedure is for a team of specialists from the medical fields involved to discuss the diagnostic and therapeutic objectives as a team. The cooperation of these specialists in a tumor conference ensures the patient the highest possible level of competence, quality and safety when it comes to deciding on and implementing diagnostic and therapeutic procedures.

What does “tumor” mean?

The term tumor is from the Latin, means “swelling or knot” and is a neutral term in medical terminology. Any mass is designated a tumor before its dignity („benign/malignant”) is known. As is the case with the other bones of the skeleton, benign or malignant tumors and malignant metastases deriving from malignant tumors with their primary location elsewhere in the body can be found in the spinal column.

How are tumors classified?

Tumors are classified according to the cell groups from which they are formed and from which they most likely derive.

Classification of a tumor as benign or malignant and the typing of the tumor to determine its cell structure are established in histological (cellular), histochemical, and immunohistochemical analyses. In these tests, proteins from the tissues can be rendered visible with the help of antibodies, allowing for conclusions about the specific tissue type present (e.g. tumor tissue type).

The benign tumors are normally easy to identify because their cells are highly differentiated, i.e. the cell group is made up of the same kind of cell and makes a homogeneous impression. The less differentiated a cell group is, the more difficult it can be to determine its dignity (benign/malignant), since different stages of cell differentiation may be present in an undifferentiated tumor cell group.

Malignant bone tumors, like benign tumors, can be classified according to where they came from as osteogenic (from bone), chondrogenic (from cartilage), or vasogenic (from blood vessels), fibrous histiocytic (from connective tissue) and hematopoietic (from bone marrow) tumors.

Which malignant bone tumors occur in the spinal column?

· Malignant osteogenic tumors

· Osteosarcoma

The onset of osteosarcoma often falls between the 10th and 20th year of life. Male children and adolescents are more often affected than females, and adult onset is much rarer.

Osteosarcomas can also develop in adults in the spinal column and pelvis as a result of radiation treatment of another tumor or in the presence of Paget's disease (bone disease characterized by degradation of bone substance).

The cause of these tumors is not yet definitively known, though growth and hormone-related factors are under discussion as possible causes. The osteosarcomas develop in the metaphyses (growth zones) of the long tubular bones or in the spongiosa (young bone substance) of smaller bones. The main localizations are the knee joint area, jawbone, humerus, pelvis, and hip areas, with less frequent occurrence in vertebrae and the small bones of the hands and feet.

Osteosarcomas show a propensity for rapid formation and dissemination of hematogenic metastases (cancer-spreading cells disseminated via the bloodstream) to the lungs, other skeletal bones and, less frequently, to the lymph nodes.

Treatment of osteosarcomas consists of high-dose chemotherapy and surgical removal of the tumor.

· Aggressive osteoblastoma

Aggressive osteoblastomas are rare malignant tumors characterized by slow growth that affect the spinal column at the vertebral arches and pedicles as well as the long tubular bones (humerus, femur).

· Malignant chondrogenic tumors

· Chondrosarcoma/chondromyxoid sarcoma

Highly differentiated chondrosarcomas grow slowly. Undifferentiated tumors can grow to considerable size within a few months, forming poorly vascularized, cartilaginous tumor tissue.

Onset of this tumor type is frequently between the 30th and 60th years of life, and men are more frequently affected than women. Chondrosarcomas are frequently observed in the ribs, the pelvis, and long tubular bones, more rarely in the spinal column. Metastasization (metastatic spread) occurs in the lungs and adjacent lymph nodes. Chondrosarcomas show little radiosensitivity or reaction to radiation therapy and chemotherapy. The therapy of choice is therefore the most radical surgical removal of the tumor tissue possible.

· Malignant vasogenic tumors

· Hemangiosarcoma/angiosarcoma/hemangioendothelioma

These rare tumor types derive from the blood vessels and occur mainly in the skin, liver, female breasts, and bones. Treatment consists of surgical removal of the tumor, chemotherapy or radiotherapy.

· Malignant fibrous histiocytic tumors

· Fibrosarcoma

Fibrosarcomas derive from connective tissue. They form tumor clusters of collagenous fibers without bone or cartilage growth that dissolve bony substance (osteolysis). Therapy consists of surgical removal of the tumor, since this type shows little response to chemotherapy or radiotherapy.

· Malignant fibrous histiocytoma

This tumor type presents a wide variety of histological patterns. It is frequently observed to occur after previous damage to the bone substance (e.g. Paget's disease or high-dose radiotherapy). The tumor results in extensive osteolysis of the affected bone. Treatment consists of surgical removal and chemotherapy.

- Malignant hematopoietic tumors

- Plasmocytoma (multiple myeloma, morbus Kahler)

Plasmocytoma are the type of malignant tumors most frequently observed in the spinal column. Disease onset in most cases is after the 50th year of life, and men are more frequently affected than women.

A plasmocytoma is an uncontrolled proliferation of plasma cells in the bone marrow, interfering with blood cell production. Plasma cells are elements of the immune system that are produced in the bone marrow.

The degenerated plasma cells cause the affected bone to dissolve (osteolysis). This process of degradation of bony substance releases calcium, significantly raising blood calcium levels (hypercalcemia).

The proliferating plasma cells displace the healthy red and white blood cells, resulting in anemia, susceptibility to infection, and a general weakening of the immune defenses. Gamma globulin levels are elevated, paraproteins (Bence Jones proteins) are found in the urine.

Diagnosis is confirmed by a bone marrow biopsy.

The most frequent localizations are vertebral bodies, ribs, clavicle, cranium, pelvis, and femur.

Plasmocytomas are treated with chemotherapy and radiotherapy. Surgery may be indicated for single myelomas on the spinal column, or in cases of vertebral collapse or imminent paraplegic symptoms.

- Ewing's sarcoma

Ewing's sarcoma occurs in children and adolescents and is the most aggressive of all bone tumors. Ewing's sarcoma is observed mainly in the long tubular bones, pelvis, and vertebral bodies. This tumor type grows rapidly and disseminates metastases into the skeleton and lungs from an early stage. Ewing's sarcoma is readily radiosensitive and also responds to chemotherapy. Surgical tumor removal may become necessary depending on local findings.

- Non-Hodgkin's lymphoma (NHL)

Malignant lymphomas are malignant tumors of the lymphatic system. This tumor type causes degeneration and pathological proliferation of lymphocytes, the cells responsible for the body's immune defense.

Since non-Hodgkin's lymphomas may arise from lymphocytes at various different stages of development, they are classified in different groups (B- and T-cell lymphomas, low and high malignancy NHL).

Since the tumor cells are disseminated in the lymphatic system, they can occur practically anywhere in the body. Treatment of these lymphomas consists of radiotherapy, chemotherapy and radioimmune therapy. A bone marrow or stem cell transplant may be useful depending on the lymphoma type.

Surgical removal of a lymphoma may also be indicated depending on the lymphoma type, localization, and disease stage.

- Malignant tumors that derive from other sources

- Giant cell carcinoma (osteoclastoma, brown tumor)

The giant cell carcinomas belong to the group of semi malignant tumors, since benign forms can rapidly degenerate into the malignant form.

Onset of this tumor type is between the 15th and 40th year of life, and women are affected somewhat more frequently than men. Giant cell carcinomas occur in the connective tissues of the bones. The osteoclasts present there disintegrate the healthy bone substance, resulting in osteolyses.

The osteoclastoma shows a proclivity to recur (recidivate) after removal and is hard to differentiate at the cellular level since its tissue structure can change. This tumor type is observed mainly in the long tubular bones, more rarely in the spinal column. Metastatic spread to the lungs is possible.

- Chordoma

A chordoma is a potentially malignant tumor deriving from the tissues of the residual chorda dorsalis (the structure from which the vertebrae develop in the embryonic stage). This tumor is observed almost solely in the base of the skull, the sacrococcygeal region, and the cervical spine.

Onset is in middle age. Chordomas cause extensive osteolysis. They show little if any response to radiotherapy and chemotherapy, which is why surgery may be indicated, depending on local findings.

What symptoms may be caused by malignant tumors of the spinal column?

The type and severity of the symptoms depend on tumor spread and location. Since the presence of a tumor does not cause specific symptoms, it can prove difficult to differentiate back pain caused by tumor disease from pain deriving from other causes, such as diseases of the spinal column involving wear, simply because the symptoms may be similar.

- General symptoms, e.g.

- Fever
- Weight loss
- Nocturnal sweating
- Exhaustion
- Drop in performance

- Pain with different causes and qualities

- Dull constant pain at level of tumor
- Periosteal pain (periosteum) caused by raising and stretching of the periosteum as a result of the destruction of the cortical layer (outer wall of the vertebra) by the tumor
- Local pressure or percussion pain
- Pain at rest
- Stress-dependent pain
- Nocturnal pain
- Painful spinal column movement restrictions

- Lymph node enlargement

- Neurological disturbances due to compression of the spinal cord or spinal nerves

- Radicular symptoms resulting from pressure exerted by the tumor on the spinal nerve roots. Compression of the posterior spinal nerve root results in sensory defects in the corresponding area of distribution with painful dysesthesias (impairment of sensation). Pressure on the anterior spinal nerve root causes sensomotor defects with paralyzes and atrophy of the muscles in the corresponding areas of distribution.
- Paraplegic symptoms
Rapid tumor growth may cause acute, complete paraplegia.
Pressure on the posterior white columns of the spinal cord results in disturbances in depth sensitivity and gait, and changes in sensation of pain and temperature.
If the pyramidal (corticospinal) tract is damaged by tumor pressure on the spinal cord, a muscular weakness may develop in the legs accompanied by a sense of tiredness and temporary paralytic symptoms.
- Dysfunctions of bladder and colon function
- Sexual dysfunction
- Changes in reflexes (enhanced, reduced, absent)

- Instability of affected mobile segment due to
 - Increasing destruction of the vertebra affected by tumor disease
 - Pathological fracture of the destabilized vertebra
- Symptoms deriving from the organ systems in which the primary tumor is located and metastatic spread to the spinal column (gynecological symptoms, gastrointestinal symptoms, abnormalities in the urogenital system, lungs, thyroid gland and prostate).

How are malignant tumors of the spinal column diagnosed?

Malignant primary tumors of the spinal column are often diagnosed “incidentally” within the framework of an x-ray examination to clarify “back pain.”

It is important to do a complete diagnostic workup so that the dignity (benign/malignant) of the vertebral finding can be confirmed and clear evidence can be obtained as to whether metastases from the cancer have already disseminated to other organ systems (lungs, liver, lymph nodes). This information then serves as the basis for any further therapy.

The following examination methods can be used to obtain an exact diagnosis:

- Medical history and clinical examination
 - Onset and nature of symptoms? (acute/gradual onset)
 - Did the symptoms occur without any apparent cause?
 - Accident traumas in medical history?
 - Any history of spinal column or back symptoms?
 - Is spinal mobility restricted?
 - Where is the pain?
 - Describe the quality of the pain (dull, burning, continuous, intermittent, dependent on stress load or postural position)?
 - Any soft tissue swelling?
 - Any lymph node swelling?
- Neurological examination
 - Are there any sensory or motor dysfunctions?
 - Does patient limp in an attempt to relieve pain, or due to paralysis, or leg shortening?
 - Are there any signs of bladder, colon or sexual dysfunction?
 - Are the muscles normal or is muscular atrophy evident?
 - Have the reflexes changed?
- Instrumental imaging diagnostics
 - Conventional x-ray images

Conventional x-ray images in 2 planes with oblique or direct images may provide valuable initial information for an first diagnosis.

It is possible to assess the location and spread of the tumor, the nature of the bony structure of the vertebra, and the height of the intervertebral space. The location of the tumor within the vertebra provides initial evidence of its dignity (benign/malignant), since benign processes, with the exception of hemangioma and eosinophilic granuloma, are usually found in the posterior portions of the vertebrae and malignant tumors are usually found in the anterior portions.

- Computer tomography (CT)
Using this layered imaging technique, tumorous changes in the bony vertebral structure can be visualized. Different sectional image layers are combined to create three-dimensional reconstructions of local findings. Computer tomography is used in precision puncturing of the suspicious tissues or for imaging of narrowed spinal canal sections with the help of a contrast agent (CT myelography).
- Magnetic resonance tomography (MRT, MRI)
Magnetic resonance tomography is highly suitable for assessing the location of the tumor in relation to the spinal cord and spinal nerves, possible infiltration of neighboring soft tissues, and mass displacement or ingrowth of the tumors into vessels in fine-layered images.
This technique is now considered the most useful of all for diagnosing tumor diseases, and also for differential diagnostics to distinguish them from other diseases of the spinal column. Another important field of application for MRT is in monitoring the disease's course after surgery, radiation therapy, or chemotherapy.
- Nuclear medicine examination methods
 - 3-phase skeletal scintigraphy
In this method, the patient is injected with a radioactive marker (technetium-99m methylene diphosphonate) that then accumulates in bones at areas where metabolic activity levels are elevated. The entire bony skeleton is portrayed and the areas with elevated metabolic levels are clearly distinguishable from normal structures, thus providing an overall simultaneous view of all areas with raised metabolic activity levels.
This method is nonspecific, i.e. any and all areas of high-level bony metabolism are shown. Differentiation between benign and malignant tumors, active arthrosis, or an infection of a vertebra can only be obtained using the other diagnostic methods.
 - Positron emission tomography (PET)
Preceded by administration of a radioactively marked substance, this method renders increased levels of metabolic activity in the body (e.g. the elevated metabolic levels in a tumor) visible. Modern PET devices are coupled with CT scanners. This "two-in-one scanner" creates images using both CT and PET technology that are then compiled by computer to create an image that provides the needed information.
 - Single photon emission computer tomography (SPECT)
This nuclear medicine examination method, combined with spiral computer tomography and the administration of various agents with low-level radioactivity, can make changed metabolic processes in the body down to the molecular level visible. This combination of the two methods unifies the data obtained in the SPECT examination with the layered spiral CT images, allowing for the exact localization of regions of the body with pertinent anomalies.
- Myelography
With the injection of a contrast agent into the spinal canal, myelography can make changes that are narrowing or compressing the spinal nerves (e.g. tumor compression, intervertebral disc prolapse) visible. The contrast agent is distributed throughout the entire spinal canal by shifting the position of the patient on the examination table. A dynamic examination in motion can be done using fluoroscopy. Myelography is usually followed by a CT scan.
- Angiography
If a precise image of tumor vascularization is required as a basis for surgical planning and MRT and CT cannot provide reliable results, a contrast agent-based image of the arterial vessels can be obtained by this method, proving exact information concerning the vascularization of the tumor and the position of the tumor in relation to major vessels.

- Sonography

An ultrasonic examination, of the abdominal cavity in particular, provides for a rapid indication of the possible presence of liver tumors, kidney or adrenal tumors, or suspected lymph node changes along the major vessels of the abdominal cavity.

- Biopsy and examination of tissues at the cellular level

In a biopsy, various methods are employed to remove tissue from a suspicious area. These tissue samples can then be examined under a microscope.

This examination method facilitates a reliable assessment of the dignity (benign or malignant) of a tumor, so that further therapeutic steps can then be taken.

There are various biopsy methods:

- Closed methods

In fine needle or punch biopsy, a small amount of the suspected tissue is removed under anesthesia.

By examining this tissue sample under a microscope, it is possible to arrive at an exact histological (microscopic structure of tissue) diagnosis (tumor type, benign/malignant).

These punctures are minimally invasive in nature and are usually done under CT monitoring.

- Open methods

Excision or incision biopsy involves partial or complete removal of tissue portions altered by tumor activity under anesthesia, followed by histological analysis of the tissue.

- Laboratory diagnostics

Laboratory diagnostics are generally not suited to the confirmation of the presence of a tumor. Some laboratory parameters are nonspecific, i.e. they can also be changed by other diseases.

- Blood sedimentation rate (BSR)

- C-reactive protein (CRP)

- White blood cell count (leukocytes)

These inflammation parameters can be elevated in tumor diseases, but this may also be the case with other kind of infection.

Tumor markers are proteins that occur in low concentrations in blood plasma, where they can be measured.

They are produced by tumor cells, but sometimes by normal cells as well.

While elevated concentrations of various tumor markers may be an indicator of the potential presence of certain type of tumor, this evidence is not conclusive.

Known tumor marker include:

- Alpha-fetoprotein (AFP) as an indicator for hepatic (liver) carcinoma

- Neuron-specific enolase (NSE) as an indicator for a parvicellular bronchial carcinoma or neuroendocrine tumors

- Prostate-specific phosphatase (PSA) as an indicator for prostate carcinoma

- Monoclonal antibodies from the group of cancer antigens (CA) may, depending on the existing CA type, provide evidence of tumors of the mammary glands, the pancreas or the stomach.

- Carcinoembryonal antigen (CEA) is an indicator for tumors of the gastrointestinal tract

How is diagnostic staging of bone tumors and bone metastases done?

Once a tumor is found in a bone or other organ, the treating physician must quickly gain an overall picture that includes the following factors in order to classify the newly found tumor according to stage (grading):

- Dignity, i.e. is the tumor benign or malignant?
Final confirmation of this can be obtained by microscopic analysis of a tissue sample at the cellular level (histology).
- In this analysis, the status of the tumor cell groups can be determined, i.e. to what extent the tumor cell groups deviate from healthy, differentiated cells. This procedure is known as tumor grading. It provides valuable information as to the aggressiveness, growth, and metastatic spread potential of the tumor. The grades are classified from G1 (well differentiated) to G4 (undifferentiated). The more undifferentiated tumor tissue is, the more malignant the tumor is.
- Tumor location and spread
CT and MRT scans can be used to determine the location and spread of the tumor and its relation to adjacent tissue structures.
- Are metastases from the tumor present in other organ systems (lungs, liver, bones)?
Whole body skeletal scintigraphy, MRT, and CT reveal whether, and where, metastatic spread has taken place. Accurate knowledge concerning these factors is decisive for developing an individual therapeutic strategy and the prognosis of the course of the tumor.

Is there a system to classify malignant bone tumors or bone metastases (TNM classification)?

The TNM system is used for all malignant tumors with the exception of leukemia and malignant lymphomas. This system can be used to assess individual cases of tumor disease.

The TNM system is internationally standardized. It provides support to practicing physicians after diagnosis and throughout the course of the disease by defining a “common language”:

The three letters stand for:

- | | |
|------------------|--|
| · T (tumor) | Tumor extent or size of primary tumor |
| · N (node) | Are there any lymph node metastases? |
| · M (metastasis) | Has metastatic spread from the primary tumor occurred? |
| · G (grading) | How is the differentiation of the tumor tissue graded? |

The letters T, N, M and G are further differentiated by adding numbers that provide information as to the size of the tumor (T1-T4), the existence and number of lymph node metastases (N0-N3), presence or absence of metastatic spread to other organ systems (M0 or M1) and the degree differentiation (grade) of the tumor tissue (G1-G4).

If it is not possible in the diagnostic process to provide reliable information on one of the three factors in the TNM system or grading, the letter X is added.

“MX” would therefore signify that no reliable data on the presence of metastases can be provided.

Example of TNM classification of a primary bone tumor of the spinal column:

T1N1M1G4 would mean:

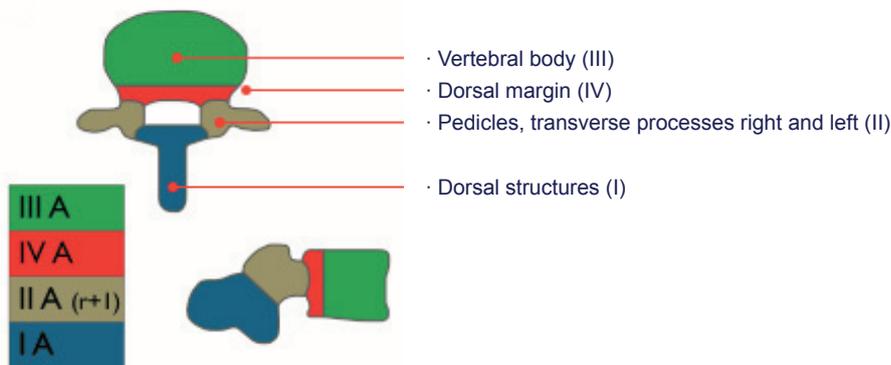
- T1: The tumor has broken through the corticalis (hard bony outer wall) of the vertebra and is infiltrating the adjacent tissue
- N1: Regional lymph node metastases are present
- M1: Confirmed metastatic spread of the tumor to lungs, liver, or other bones
- G4: The tumor tissue is undifferentiated, i.e. highly malignant

Is there a classification system that designates the location of a tumor in relation to surrounding structures, providing a surgeon with information for planning a possible surgical procedure?

In 1991, Weinstein introduced a classification system in which a tumor is grouped in terms of 4 different zones: Zone I corresponds to the dorsal (posterior) structures of the vertebra, Zone II includes the pedicles and the right and left transverse processes, Zone III includes the vertebral bodies and Zone IV the dorsal margin of the vertebral body. The letters A, B and C are also used to differentiate whether the tumor is in the bone (intraosseous = A) or outside of the bone (extraosseous = B) and whether metastatic spread has already occurred (= C).

Example: the classification I A would mean that the tumor is present inside the dorsal vertebral structures

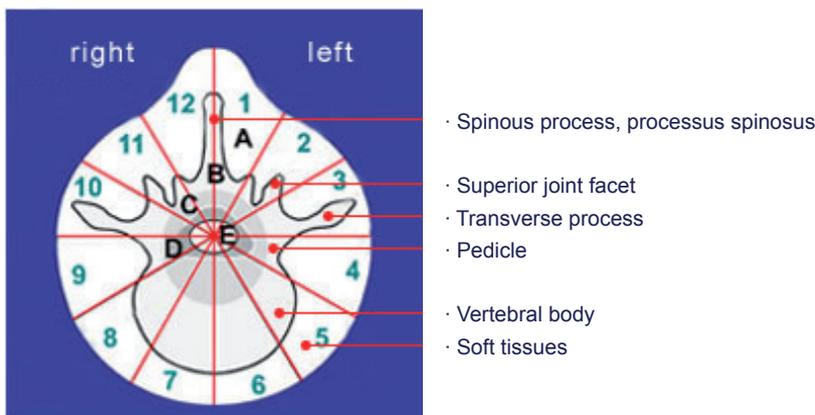
• Weinstein classification (1991)



In 1997 the Weinstein classification was further refined and introduced as the Weinstein-Boriani-Biagini tumor staging system.

The graphic presentation shows the vertebra divided into 12 radial segments in clockwise order. There are also 5 additional concentric areas A-E from the outer area A (soft tissues external to the vertebra) to the interior area E (spinal canal with spinal cord). Together, these coordinates facilitate an exact localization of the tumor.

• Weinstein-Boriani-Biagini classification



Using the above-mentioned classification system, the surgeon has access to valuable information regarding the differentiated allocation of the tumor to the areas of the vertebra and its surroundings, which can be used as the strategic basis for an operation.

How are malignant tumors of the spinal column treated?

Once a tentative diagnosis “tumor of the spinal column” has been reached, the dignity (benign/malignant), exact localization, existence of any metastases in other organ systems and the cellular structure of the tumor must be clarified.

If the diagnosis malignant tumor is confirmed, a therapeutic strategy must be drawn up based on the findings at hand.

Since tumor disease always comprises a complex clinical picture, the individual therapeutic strategy must be developed by a team of specialists. The cooperation of these specialists in this interdisciplinary tumor conference ensures the patient the highest possible level of therapeutic quality based on their specialist skills and knowledge. The participants in the tumor conference include surgeons as well as specialists for tumor chemotherapy (oncologists) and radiotherapy, radiologists and pathologists.

The main pillars of vertebral tumor treatment are:

- Radiotherapy
- Chemotherapy
- Pain therapy
- Tumor surgery

Malignant tumor diseases of the spinal column cannot always be healed despite surgery and supportive radiotherapy and chemotherapy.

In the spinal column in particular, the surgeon encounters limitations presented by the anatomical situation (spinal cord, spinal nerves, vascularization) when it comes to radical surgery. That is to say: not every tumor can be radically removed in the oncological sense of the word.

Tumor surgery of the spinal column adapted to the individual findings may, however, help improve the quality of life of the patient to a significant degree.

- Tumors in favorable locations can be removed completely (curative, “healing” treatment)
- If a vertebra is or threatens to become destabilized by the tumor growth, the risk of neurological defects or paraplegic symptoms may be eliminated.
- Pain can be reduced by removing the tumor or reducing the tumor mass. If surgery does prove necessary, a number of methods of tumor removal and subsequent stabilization of the mobility segment are available.

Here is a list of some of the surgical methods used frequently in our department in treatment of malignant vertebral tumors:

Tumors of the cervical spine:

- Transoral dens resection with dorsal spondylodesis
- Dorsal decompression with cervical fusion
- Ventral corpectomy with cervical spondylodesis

Tumors of the thoracic and lumbar spine:

- Corpectomy with dorsal spondylodesis

Tumors of the sacrum (os sacrum)

- Sacrum surgery with special instrumentation

What is oncological follow-up?

Malignant tumors must be monitored at regular intervals after conclusion of treatment.

Generally speaking, control follow-up examinations are carried out at 3-month intervals during the first 2 years after a tumor diagnosis is reached.

Biannual checkups follow in the 3rd to 5th years, with annual checkups beginning in the 6th year.

A number of techniques are employed in these examinations (CT, MRT, scintigraphy, ultrasound, clinical, and neurological examination) to determine whether the patient's overall condition has remained stable or if tumor growth has resumed.

Regular checkups facilitate rapid intervention should tumor growth reoccur.