Spinal Disorders

Fundamentals of Diagnosis and Treatment

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Primary Tumors of the Spine

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Core Messages

✔ Primary spine tumors are relatively rare
✔ Cancer is a genetic disease
✔ The acquired capabilities of cancer are: self-sufficiency to growth signals, insensitivity to anti-growth signals, tissue invasion and metastasis, limitless replicative potential, sustained angiogenesis, evading apoptosis
✔ Spine tumors are classified based on the histology
✔ Pain, spinal deformity, and neurologic deficits frequently are presenting symptoms
✔ Age and location are important parameters for establishing a differential diagnosis
✔ CT and MRI are essential for systemic and surgical staging
✔ Biopsy is required to establish the tissue diagnosis

✔ The biopsy has to be placed so that it does not compromise subsequent surgical resection
✔ Do not rely completely on the result of the biopsy – the final histology may be different
✔ The "wait and see" approach is very rarely indicated
✔ Conservative treatment is only indicated for benign tumors and in asymptomatic patients
✔ Malignant tumors in general are treated surgically
✔ In sensitive tumors, chemo- and radiotherapy are considered as an adjuvant treatment
✔ The goal of surgery is to remove the primary tumor in its entirety followed by stable reconstruction of the spine

Epidemiology

Approximately 2 000 new cases of bone cancer and 6 000 new cases of soft tissue tumor are diagnosed in the United States each year [30]. Of these, only about 5 % involve the spine. The incidence of primary spinal tumors has been estimated at 2.5 – 8.5 per 100 000 people per year [15]. Tumors of the lymphoid system, e.g., plasmocytoma, are generally considered in the discussion of spine tumors although they are tumors of the **lymphoreticular system**. Some bone tumors have a special predilection for the vertebral column (e.g., osteoblastoma), while others occur exclusively in the spine (e.g., chordoma). There are two important clinical features to be considered when evaluating the potential of malignancy of a spine lesion, i.e.:

Primary spinal tumors are rare

Plasmocytomas are tumors of the lymphoreticular system
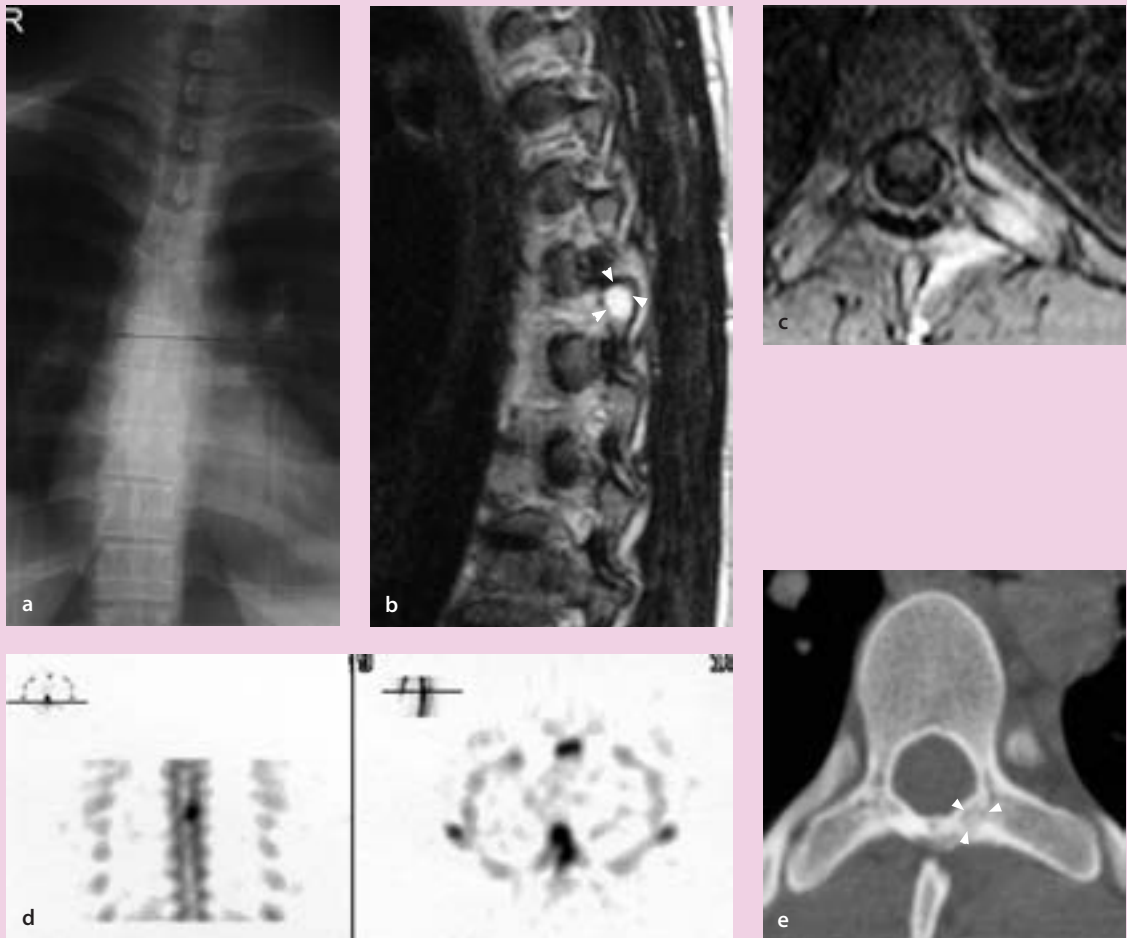
- age
- location

In **children younger than 6 years** of age, most spinal tumors are malignant, e.g.:

- neuroblastoma
- astrocytoma
- sarcoma (less commonly)

However, benign spinal tumors outnumber malignant tumors by a ratio of 2 : 1 among children of all ages.

Case Introduction

A 20-year-old girl presented with severe intermittent dorsal pain with occasional radiation into the ribcage. The patient was unsuccessfully treated with physiotherapy. The pain got progressively worse particularly during the night; she was then referred for further evaluation. Standard radiographs of the thoracic spine were unremarkable although it was noted that she had a significant shift to the left side (**a**). The patient noticed a decrease of symptoms when she took NSAIDs. An MRI scan demonstrated increased signal intensity in the posterior elements of T7 on the left side (**b**, **c**). The bone scan showed increased uptake in that region (**d**). A CT scan showed the typical features of an osteoidosteoma with a hypodense lesion with a nidus (**e**). The lamina was exposed for an excision biopsy. However, since the nidus was clearly visible it was decided to remove it by curettage. The bed of the nidus was cleaned with a high-speed air drill. The patient's symptoms completely disappeared after the operation and she remained painfree during follow-up.

In **adults older than 35 years**, most spinal tumors are:

- metastatic adenocarcinoma
- multiple myeloma
- osteosarcoma

Spinal tumors exhibit a specific anatomic predilection

Spinal tumors demonstrate a specific anatomic predilection. Osseous tumors of the anterior vertebral body are most likely metastatic lesions, multiple myeloma, histiocytosis, chordoma, and hemangioma. The most common osseous spinal tumors involving the **posterior elements** are:

- aneurysmal bone cysts
- osteoblastoma
- osteoid osteoma

Malignant osseous tumors occur much more commonly in the anterior than the posterior spinal elements.

Tumor Biology

Molecular Tumor Biology

Recent advances in basic research of musculoskeletal tumors revealed that the sheer complexity of the molecular process of carcinogenesis may be conceptually reduced to a small number of molecular, biochemical, and cellular traits that are shared by most if not all types of human cancer. Hanahan and Weinberg [25] described the **hallmarks of cancer** which represent a fundamental concept that governs the development of malignant transformation. It is hypothesized that a developing cancer may represent the interplay between these fundamental concepts. The acquired capabilities of malignant tumors are shown in Fig. 1.

Whenever a cell divides, the telomeres (i.e., ends of chromosomes) shorten until a point of no return and the cell then dies. Cancer cells can switch on a protein component of telomerase that allows them to maintain their telomeres and to divide indefinitely. The normal cell has a built-in cellular program to die or undergo apoptosis, respectively. For a cancer cell to become immortal, it needs to escape **apoptosis**. A malignant cell needs to have the capacity to mimic extracellular growth signals, for example by activating mutations, in order for the tumor to grow. Malignant tumors need to produce their own **blood supply** if they are to grow beyond a certain size. The nature of the angiogenic switch is still unclear, but endothelial cells must be recruited, grow, divide, and invade the tumor to form blood vessels. A further capacity of a malignant cell is to acquire the poten-
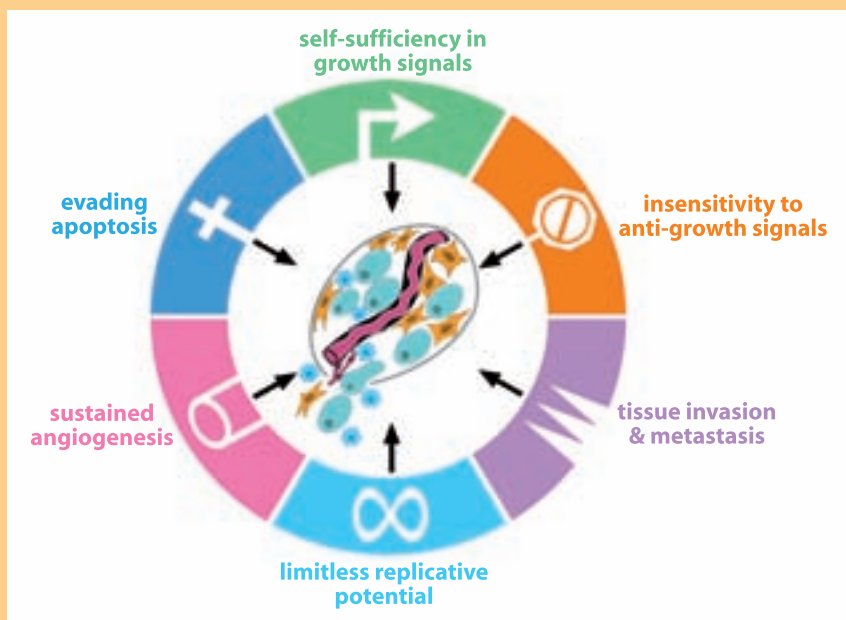

Figure 1. The hallmarks of cancer

According to Hanahan and Weinberg, most if not all cancers have acquired the same set of functional capabilities during their development, although through various mechanistic strategies. (Redrawn from Hanahan et al. [25] with permission from Elsevier).

tial to break away from the original tumor mass, resist anoikis (apoptosis that is induced by inadequate or inappropriate cell-matrix interactions) and crawl through the extracellular matrix into blood or lymphatic vessels in order to recur and survive in a distant organ.

The hallmarks of cancer help us to understand the complexity of such a disease in terms of a relatively small number of underlying molecular principles. Obviously, these hallmarks only represent a working model. An emerging paradigm is that this set of principles has a specific mechanism for each tumor type so that each tumor bears its own molecular circuitry that needs to be characterized individually.

The hallmarks represent a concept of carcinogenesis

Pathways of Metastasis

More than a hundred years ago, Sir Stephen Paget first launched the "seed and soil" hypothesis, asking the question: "What is it that decides what an organ shall suffer in case of disseminated cancer?" His answer is basically still valid today: "The microenvironment of each organ (*the soil*) influences the survival and growth of tumor cells (*the seed*)."
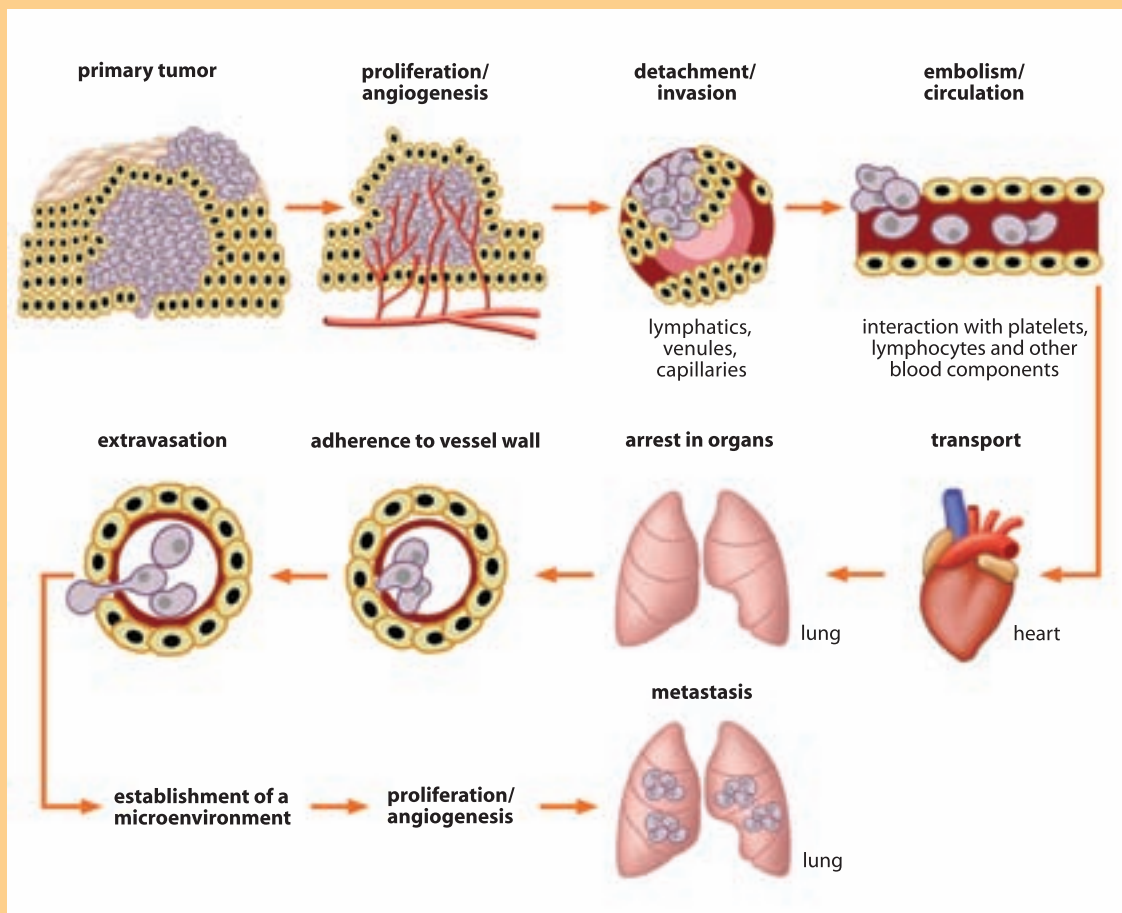

Figure 2. The metastatic cascade

The schematic drawing exemplifies the main steps in the formation of a metastasis. (Redrawn from Fidler [18] with permission from Macmillan Publishers Ltd.).

The process of **metastatic spread** of a primary tumor can be described in the following steps (**Fig. 2**):

- local tumor proliferation
- angiogenesis
- migration and invasion
- intravasation
- adhesion
- extravasation
- migration and invasion
- metastatic growth in target organ

In the metastatic process, the primary tumor proliferates locally until it reaches a size when nutrition cannot be provided by diffusion alone. Neovascularization or angiogenesis is therefore present at an early stage in a tumor. The tumor cell then detaches from the neighboring cells and invades the surrounding normal tissue. It seeks access to the blood and/or lymphatic system (**intravasation**), where it gets distributed in the body until it adheres in the capillaries of the target organ. The metastatic tumor cell then crawls through the vessel wall (**extravasation**) and invades the tissue of the target organ, where finally it may grow into the metastatic nodule. It is not yet entirely understood how these processes are governed. Originally, it was assumed that metastasis is the clonal expansion of a pri-
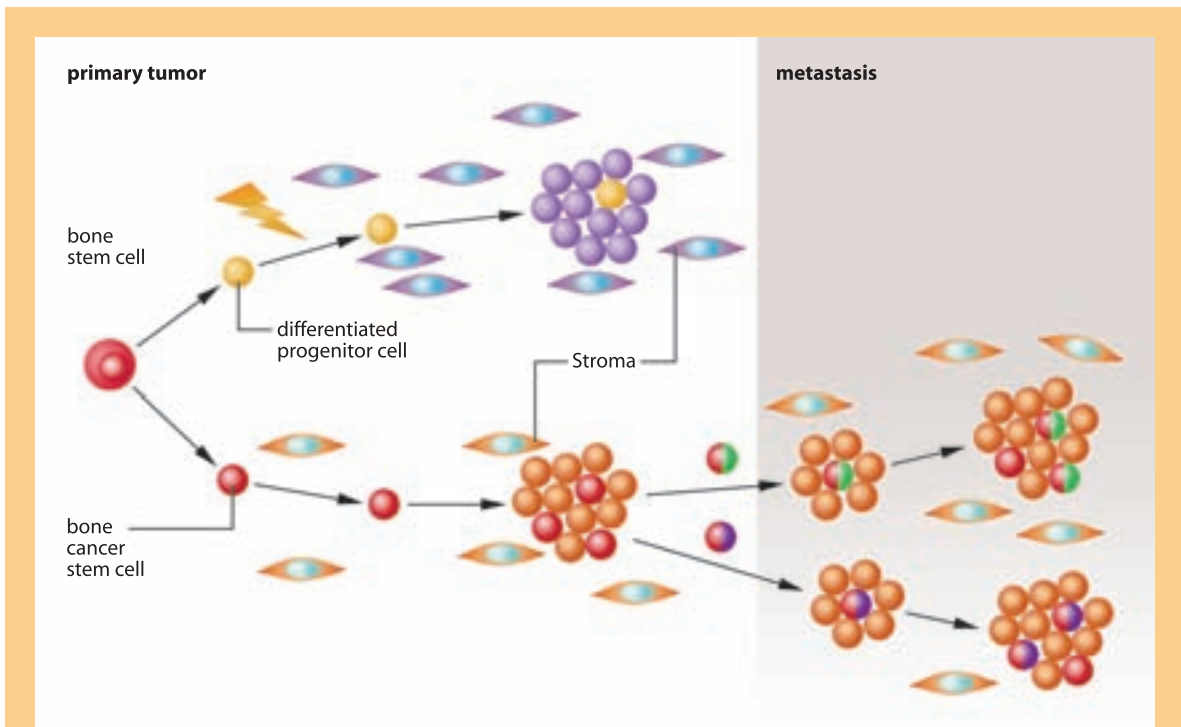
Stem cells appear to play a key role in metastasis

Figure 3. Evolution of the cancerous bone cell

Oncogenic mutations may occur in bone stem cells (*red*) and can cause the transformation to a bone cancer stem cell, generating "poor-prognosis" tumors (*orange*). Mutations which occur in differentiated progenitor cells (*yellow*) may form a non-metastatic "good-prognosis" bone carcinoma (*pink*). Under the influence of stromal fibroblasts, only the population of bone cancer stem cells has the ability to metastasize. There might be variant cancer stem cells that differ in their tissue selectivity for metastasis, expressing an additional tissue-specific profile (e.g., *green* liver, *purple* lung). (Redrawn and adapted to bone from Weigelt et al. [42] with permission from Macmillan Publishers Ltd.).

mary tumor cell. Microarray analyses revealed that for several cancers, the expression profile of a primary tumor is indifferent to its metastatic site, thus in contrast to the clonal expansion theory. The current theory implies that stem cells may play an important role. The current model of metastasis synthesizes the **clonal expansion theory**, the expression profiles and stem cells. Oncogenic mutations in stem cells cause transformation, thereby generating "poor-prognosis" tumors. However, mutations occurring in differentiated progenitor cells might form a non-metastatic good-prognosis tumor that does not metastasize. In the metastatic poor-prognosis tumors, under the influence of stromal fibroblasts, only the populations of stem cells have the ability to metastasize (Fig. 3). There might be variant stem cells that differ in their tissue selectivity for metastasis, expressing an additional tissue-specific profile. At the site of metastasis, the disseminated cancer stem cells would again induce a similar stromal response as in the primary tumor.

Histology and Biology of Spinal Tumors

Spine tumors are classified according to their **histology**. Based on the age of the patient, the anatomic location of the lesion, supplemented by modern imaging, and tumor histology, the **biological behavior of the tumor** can be determined (Table 1).

Table 1. Primary benign spinal tumors				
Lesion	Age	Location	Histology	Imaging
Osteoidosteoma	second decade	posterior elements (75%)	vascularized connective tissue, nidus surrounded by reactive cortical bone	radiolucent nidus with surrounding sclerosis, rarely extended to vertebral body, epidural or paraspinal spaces
Osteoblastoma	Second and third decades	posterior elements; equally distributed in the cervical, thoracic, and lumbar segments	osteoid-producing neoplasms	expansile destructive lesion partially calcified; common extension to vertebral body
Osteochondroma	third decade	exclusively posterior elements; predilection for spinous processes of cervical spine	cartilage cap with normal bone component	continuity of the lesion with marrow and cortex of the underlying bone
Hemangioma	any age; peak fourth decade	vertebral body lower thoracic-upper lumbar regions	vascular spaces lined by endothelial cells	vertical parallel densities spotted appearance on CT high signal on T1W and T2W images; involvement of posterior elements
Aneurysmal bone cyst	young patients <20 years	posterior osseous elements 60% vertebral body 40% thoracic, lumbar	cystic spaces containing blood products	lytic expansile lesion with fluid-filled levels involvement of contiguous vertebrae
Langerhans cell histiocytosis	first, second decades	vertebral body rarely posterior elements, thoracic, rarely lumbar, cervical	sheets of Langerhans cells, lymphocytes, and eosinophils	lytic lesion of the vertebral body leading to collapse

Clinical Presentation

History

A complete history, detailed general assessment and physical examination are essential for evaluating patients with spinal tumors. Patients with spinal tumors usually present with:

- pain
- spinal deformity
- neurologic deficit

Back pain is the most common symptom (**Case Introduction**) [16]. Pain in spinal tumors usually is:

Pain is the cardinal symptom

- persistent
- unrelated to activity
- worsening during rest and at night

Persistent, non-mechanical back pain must be distinguished from common back pain, which is often the opposite. **Night pain** is an important differential symptom of certain skeletal neoplasms such as osteoid osteoma and osteoblastoma.

Night pain is a warning signal

    Pathological fracture of vertebral bodies can occur and can cause severe acute pain similar to that seen in traumatic vertebral compression fractures. Spinal nerve root and cord compression from a pathological fracture or invasion of neoplasm results in local pain, radicular pain along the affected nerve roots or myelopathy [24]. Symptoms of spinal instability and neurologic compromise arise with increasing vertebral destruction and tumor expansion [14, 19].

    Malignant lesions with metastases usually cause associated systemic symptoms. Systemic symptoms usually are present in malignant lesions, especially in tumors such as:

- lymphoma
- myeloma
- Ewing's sarcoma
- tumors with metastasis

With the **progression of the disease**, patients can present with:

- weight loss
- fever
- fatigue
- general deterioration

However, these symptoms often appear late during the disease.

Physical Findings

Although spinal tumors seldom present with obvious physical findings, a **local palpable mass** may be present in some instances. Sacral tumors like chordoma, after growth of an anterior mass, may cause bowel or bladder symptoms and may be palpable on rectal examination [16]. Benign tumors such as osteoid osteoma are often associated with **scoliosis** and typically present with paraspinal muscle spasm and stiffness. Structurally, there is absence of a lumbar or thoracic hump as in adolescent idiopathic scoliosis. The necessity for a **thorough neurologic examination** is self-evident but it usually reveals only findings in late tumor stages.

A palpable mass is rarely the initial finding

Diagnostic Work-up

Imaging Studies

The evaluation of spinal tumors includes plain radiographs, bone scans, computed tomography (CT), magnetic resonance imaging (MRI), angiography, as well as single photon emission computed tomography (SPECT) bone scanning [22] and positron emission tomography (PET) scans.

Standard Radiographs

Standard radiography is the imaging modality of first choice

Standard radiographs are still the first imaging modality used to explore the spine when a tumor is suspected and they may demonstrate the tumor lesion. **Neoplasms** in the vertebrae can **present as:**

- osteolytic (**Fig. 4a, b**)
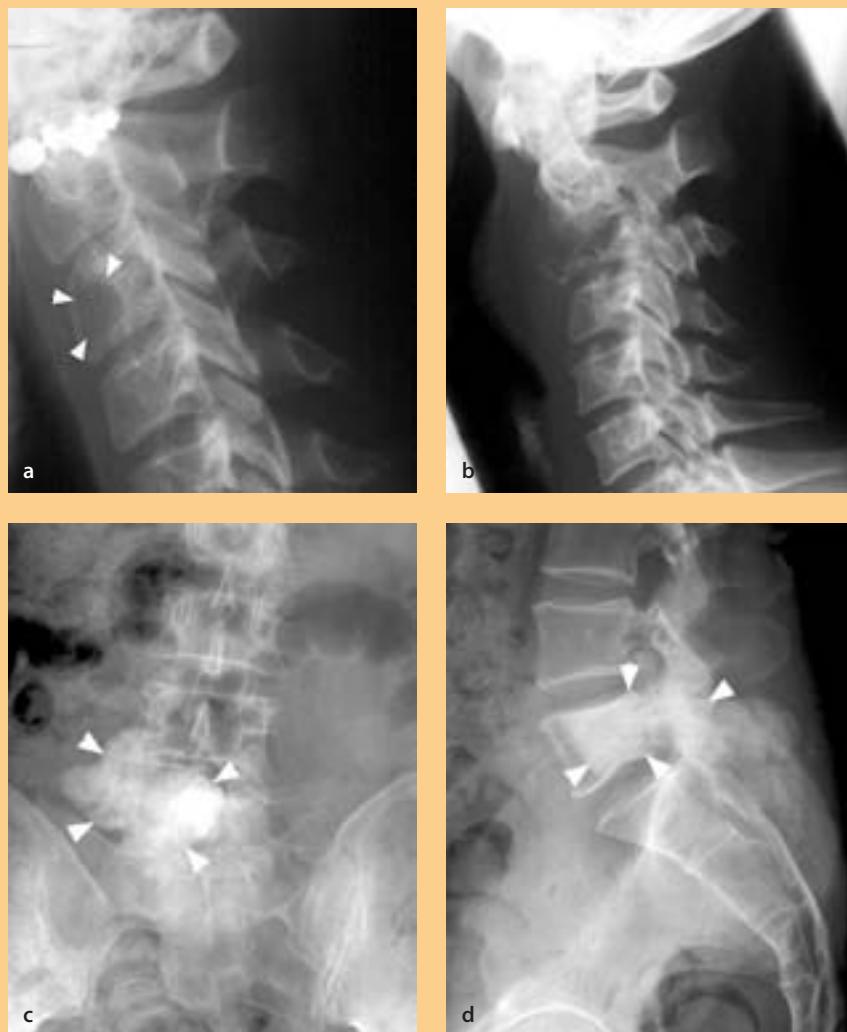- osteoblastic/sclerotic (**Fig. 4c, d**)
- mixed

Figure 4. Radiographic findings

a Osteolytic lesion in the vertebral body of C3. **b** This lesion was primarily overlooked and progressed to a severe destruction of the vertebral body of C3 with kyphotic deformity (histology: chordoma). **c, d** AP and lateral radiographs show a dense, sclerotic bone lesion with extension in the paraspinal muscles (*arrowheads*) on the right side (histology: osteosarcoma).

Benign tumors such as osteoid osteoma and osteoblastoma frequently are seen as sclerotic lesions in the posterior elements of the spine, with a central lytic area surrounded by reactive bone [39]. Lytic destruction of pedicles with the **winking owl sign** (see Chapter 34 , Case Study 2) seen on an anteroposterior view is the most classic early sign of vertebral involvement by malignant lesions, although the vertebral body typically is affected first. Before changes can be recognized radiographically, 30–50% of a vertebral body must be destroyed. In contrast, slight lysis of the pedicle can be seen early on the AP radiographs [26]. It is difficult to differentiate pathological compression fracture secondary to tumor from compression fractures of osteoporosis (Case Study 1). This differential diagnosis is always prompted when osteoporotic spine fractures are diagnosed. The intervertebral disc is usually preserved in patients with neoplasm. This helps in differentiating tumors from pyogenic infection where the disc is frequently destroyed along with the adjacent vertebral body [6]. Sometimes, a soft tissue shadow can be seen on the radiographs extending from a vertebral body lesion through the outer cortex.

Malignant neoplasm usually preserves the intervertebral disc

Lytic processes become visible on radiographs not before 30–50% of the bone is destroyed

Magnetic Resonance Imaging

MRI should be used to fully define the extent and nature of the lesion [7] and is recommended for investigating the suspected lesion in terms of:

- spinal level
- extent of suspected lesions
- vertebral bone marrow infiltration
- infiltration of the paraspinal soft-tissues (muscles, vessels)
- infiltration of the nerve roots, thecal sac, and spinal cord

Generally, MRI is a very sensitive imaging modality for detecting alterations of the bone marrow, but it does not allow a type specific diagnosis. The only exception may be a benign cavernous hemangioma. This lesion is unique in that it shows increased signal intensity relative to the bone marrow on T1W and T2W images, allowing a diagnosis with a very high probability (Fig. 5). MRI features of other tumors are not characteristic and MRI can at best narrow the differential diagnosis (Fig. 6, Tables 1, 2). Contrast enhancement is useful to detect a strong vascular uptake which can prompt an angiography. It is particularly useful for assessing the response to chemotherapy. Diffusion weighted MRI may potentially be capable of detecting and quantifying the amount of tumor necrosis after neoadjuvant therapy, but it is premature to finally conclude on this possibility [32].

High signal in T1W and T2W images indicates an hemangioma

Computed Tomography

In general, CT is more reliable in demonstrating the cortical outlines of bone and calcification in comparison to MRI. It can better show the extent of the tumor destruction (Fig. 7). Occasionally, CT allows the direct demonstration of the tumor, e.g., in case of an osteoidosteoma (Case Introduction). In terms of tumor biopsies, CT allows accurate assessment of proper needle placement during needle biopsies. However, in general, CT is not as sensitive as MRI in the detection of both metastatic disease and primary malignant bone tumors [1, 2, 13].

CT can better show the extent of bony destruction

Case Study 1

A 72-year-old male presented with acute onset of thoracolumbar back pain after an unusual movement. The pain was worse on motion and the patient could not be mobilized. An initial lateral radiograph demonstrated compression fractures at L1 and L2 (a). Non-operative treatment failed and the patient was referred for a vertebroplasty. An MRI investigation was done showing fresh compression fractures at L1 and L2 and older endplate fractures of L4 and L5. Note the bone marrow changes which are hypointense on the T1W image (b) and the hyperintense signal intensity on the T2W image (c). The signal intensity increase is better visible on the STIR sequence (d). The patient underwent a biportal vertebroplasty of L1 and L2, which instantaneously resolved the patient's symptoms (e, f). The patient was sent for a formal assessment of the putative osteoporosis during which a multiple myeloma was diagnosed. In retrospect, the assessment should have been done prior to the treatment by vertebroplasty although it would not have changed the indication for a vertebroplasty.
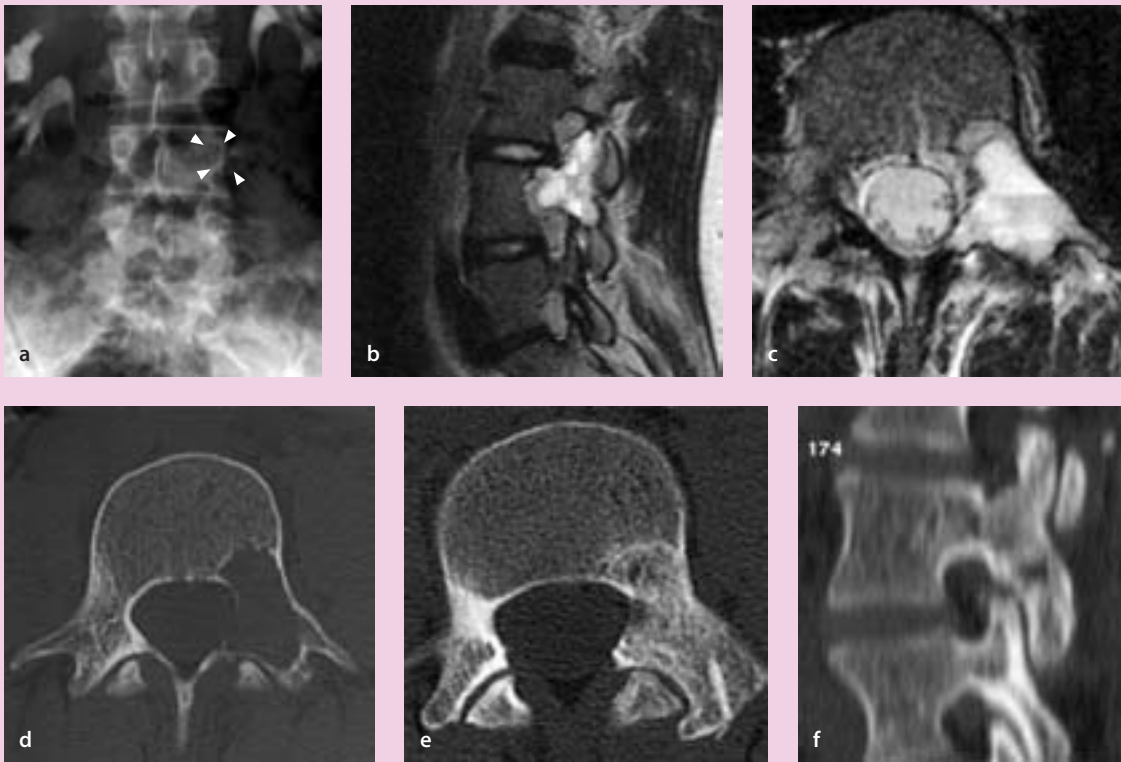
Case Study 2

A 16-year-old female underwent an i.v. pyelogram for a diagnostic assessment of recurrent urinary tract infections. The radiologist noticed a disappearance of the regular structure of the L3 pedicle on the left side (winking owl sign) (**a**). A referral and further diagnostic work-up were prompted. The MRI scan showed a large cyst without significant septal partitions on the T2W sagittal (**b**) and T2W axial (**c**) scans. No soft tissue infiltration was seen. The CT scan confirmed the diagnosis of a large cyst (**d**). The biopsy ruled out malignancy although a confirmation of the suspected aneurysmatic bone cyst was not reliably possible on the material submitted. Because of the benign lesion, an intralesional resection of the transverse process and a curettage of the superior articular process and the pedicle was done. The medial border to the thecal sac was covered with Gelfoam and the defect was filled with autologous cancellous bone. At one year follow-up the patient is symptom free and the CT scan shows a nice remodeling of the pedicle (**e**, **f**).

Radionuclide Studies

A technetium-99m (^{99m}Tc) bone scan is widely used in the initial diagnosis and follow-up of bone tumors. Technetium scans are sensitive to any area of increased osteoid reaction to destructive processes in bones (**Case Introduction**). They can detect lesions as small as 2 mm, and as little as a 5–15% alteration in local bone turnover. They can identify changes in osteolytic or osteoblastic disease 2–18 months sooner than radiographs [22, 31]. Total body scans can show most of the (also remote) skeletal lesions, and therefore are used as a screening test to determine whether a lesion is solitary or multifocal in expression and local extent. Plasmocytoma is particular in that it may be purely lytic, and therefore an ordinary scan may be negative. In these patients, ^{99m}Tc-sestamibi has been proven to very useful with a specificity of 96% and sensitivity of 92%. As an alternative, MRI may be regarded as today's standard.

A bone scan is the screening method of choice for investigating extraspinal tumor manifestation
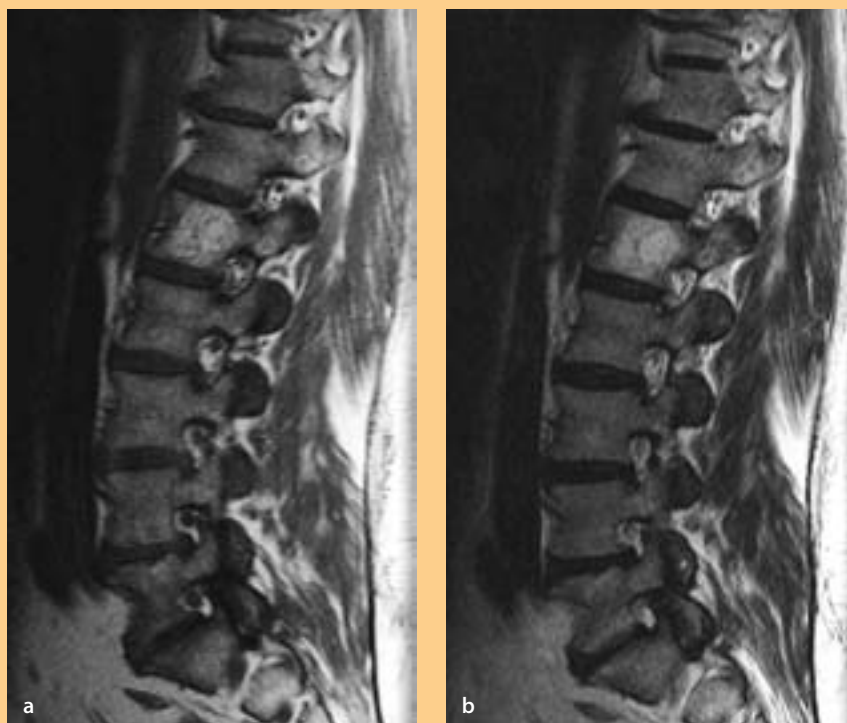
Figure 5. MRI findings of a benign hemangioma

Typical spotted bright signal intensity changes within the vertebral body of L1 on **a** T1W and **b** T2W image suggesting a benign hemangioma.

Figure 6. MRI findings in primary spinal tumors
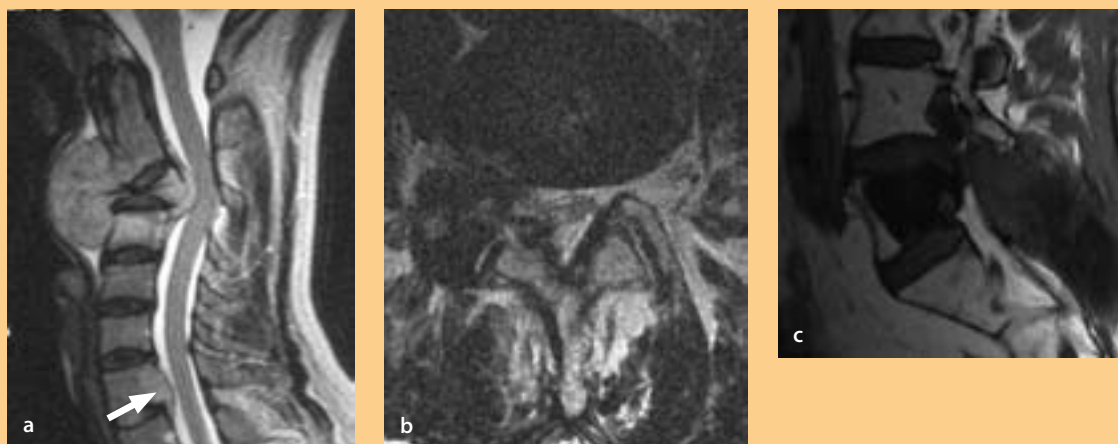
a Expansive lesion with a pseudocapsule with compression of the spinal cord and the retropharyngeal space. Note the skip lesion at the level of C7 (*arrow*, same patient as in **Fig. 4a, b**). Extension of a hypointense mass into the foramen L5 and the adjacent facet joint L4/5 on a T2W axial (**b**) and T1W sagittal image (**c**) (same patient as in **Fig. 4c, d**).

Table 2. Primary malignant spinal tumors

Lesion	Age	Location	Histology	Imaging
Osteosarcoma	Fourth decade	Vertebral body Lumbosacral region	Osteoid within sarcomatous tissue	Osteosclerotic and osteolytic areas with soft tissue component; common extension to posterior elements
Chondro-sarcoma	Fifth decade	Predilection for vertebral body Thoracic region	Hyaline cartilage with increased cellularity within myxoid matrix	Bone destruction with characteristic punctuate calcifications
Malignant fibrous histiocytoma	Second to eighth decades	Vertebral body	Mixture of histiocytes, fibroblasts and primitive mesenchymal cells	Lytic lesion with low signal on T1W and high signal on T2W images
Giant cell tumor	Third decade	Vertebral body Sacrum	Osteoclastic giant cells intermixed with spindle cells	Osteolytic geographic area with soft tissue component
Plasmo-cytoma	>40 years old	Vertebral body Thoracic and lumbar spine	Sheets of plasma cells on a delicate reticular stroma	Radiolucent areas or reduction in bone density Hypointense on T1W and hyperintense on T2W images
Ewing's sarcoma	Second to third decades	Vertebral body, lumbosacral spine	Sheets of small round blue cells	Lytic lesion, associated soft tissue mass
Chordoma	Middle-aged patients	Exclusively affects vertebral body; most often sacrum, rarely mobile spine	Lobulated mass with mucinous containing cells	Destructive midline expansile lesion with associated soft tissue mass; extension into adjacent vertebra

Figure 7. Computer tomography findings of primary spinal tumors

a Axial CT scan showing an extensive infiltration and destruction of the posterior wall (histology: plasmocytoma). **b** Axial scan indicating increased bone density in the lamina (histology: osteoblastoma).

Spinal Angiography

Spinal angiography has only rare indications for spinal lesions, usually when rich vascular structures such as aneurysmal bone cysts and hemangiosarcoma are present. Angiography is capable of showing the vascularity of all feeding and draining vessels and can be used for selective embolization of hypervascular lesions to reduce intraoperative blood loss [35].

Biopsy

One of the most important principles of tumor surgery is that of including the biopsy track with an adequate margin of healthy tissue which can be excised at definitive resection. This is sometimes impossible in the spine if an approach violating the anatomic planes is used. Poorly planned biopsies increase the local recurrence risk by tumor dissemination along fascial planes and the biopsy tract. There are **three different types** of biopsies:

- needle
- open incisional
- excisional

For tumors limited to the posterior elements, an **excisional biopsy** is both diagnostic and therapeutic. Most needle biopsies are performed under fluoroscopic or CT control [23]. In experienced hands, the accuracy rate ranges from 80 % to 90 %, but it is non-diagnostic in 25 % of patients [34]. CT guidance offers a great margin of safety for surrounding blood vessels and viscera, but complications include pain, bleeding, and pneumothorax. If **open incisional biopsy** is planned, several fundamental principles should be considered. The incision has to be planned such that it can be excised at definitive surgery. Bone windows should be small and carefully planned so that pathological fractures do not result. They are packed with bone wax and Gelfoam, hydroxyapatite or cement, depending on the surgeon's preference. Postoperative hematomas need to be avoided because they carry the potential of disseminating tumor cells along fascial planes.

Acceptable biopsy techniques for malignant tumors of the spine depend on the anatomic extent and location of the tumor. In the cervical spine, posterior tumors with or without extraosseous soft tissue involvement are easily sampled by needle using CT guidance. However, because of the predominance of benign lesions in the posterior elements and when confined to the osseous elements, **excisional biopsy** techniques may be preferred. Anteriorly, in the craniocervical region, transpharyngeal stereotactic needle biopsy is an alternative to open biopsy using the approaches for resection of tumors in this region. Tumors of the anterior thoracic spine are sampled via posterior percutaneous CT-directed needle biopsy. An open biopsy can be performed through a posterolateral approach by costotransversectomy, with careful consideration of biopsy placement. In the lower thoracic and lumbar spine, CT-guided biopsy techniques can be used; for anteriorly located lesions, transpedicular biopsy placement is possible, but later necessitates resection of the involved pedicle and soft tissue track if the lesion turns out to be malignant.

Laboratory Investigations

A complete laboratory work-up should be ordered. For patients with multiple myeloma and metastatic osteolytic lesions, serum calcium should be evaluated and the possible hypercalcemia corrected. Anemia, hypoalbuminemia and electrolyte imbalances need to be corrected before considering surgery. There are no tumor specific biochemical markers yet available for spine tumors.

Tumor Staging

A benign tumor is defined by its incapacity to metastasize, whereas a malignant tumor has the potential to metastasize. Boriani et al. [11] have suggested a surgical staging system for the spine based on Enneking's pioneering work [17] for limb lesions (Fig. 8).
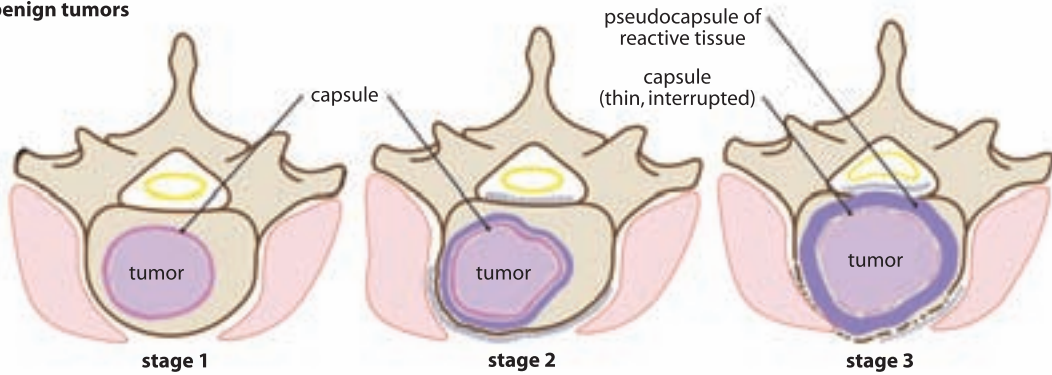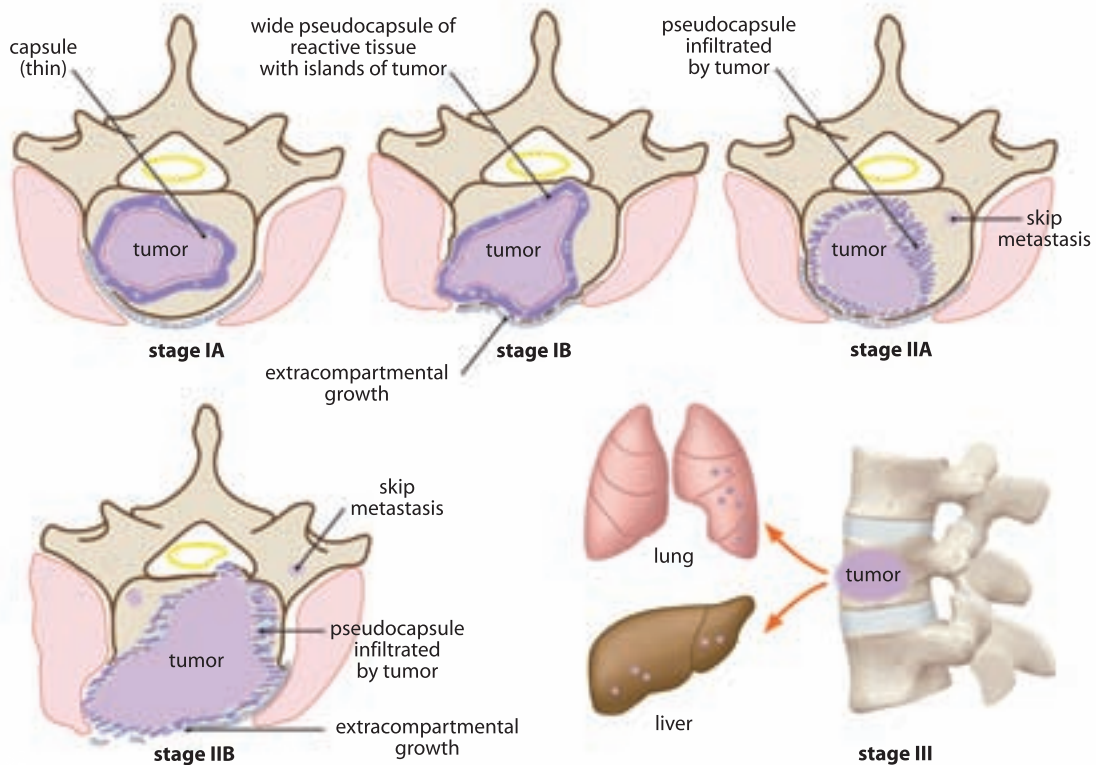
Figure 8. Staging of benign and malignant spinal tumors.

The staging considers the presence of a capsule (pseudocapsule), aggressiveness of the lesion, presence of skip lesions, extracompartmental growth, and metastases (for details see text). (Redrawn and modified from Boriani et al. [11], reproduced with permission from Lippincott, Williams & Wilkins).

Benign Tumors

Benign tumors are **staged** into:

- latent lesion
- active lesion
- aggressive lesion

Stage 1

Stage 1 (S1, **latent, inactive**) lesions include **asymptomatic lesions**, bordered by a **true capsule**. In these tumors, a well-defined margin around the circumference of the lesion is seen even on plain radiographs. These tumors usually do not grow or if they do then only very slowly. No treatment is required for S1 lesions, unless palliative surgery is needed for decompression or stabilization. Examples include hemangiomas of bone and osteochondroma.

Stage 2

Stage 2 (S2, active) lesions **grow slowly** and **cause mild symptoms**. There is a **thin capsule** around the tumor and a layer of **reactive tissues**, sometimes seen on plain radiographs as an enlargement of the tumor outline and sometimes clearly defined on MRI. Bone scans are often positive. An intralesional excision is performed with a low rate of recurrence. Examples include osteoid osteoma, aneurysmal bone cysts, and giant cell tumor of bone.

Stage 3

Stage 3 (S3, aggressive) lesions are represented by **rapidly growing** benign tumors. The **capsule** is **very thin, incomplete, or absent**. The tumor invades neighboring compartments and often has an associated wide, reactive, hypervascularized pseudocapsule, which sometimes is permeated by neoplastic digitations. There are fuzzy limits on plain radiographs; bone scans are also positive. CT scans show the tumor extension, and MRI defines the pseudocapsule and its relationship to adjacent neurologic structures. Intralesional curettage is often not enough and is associated with a high recurrence rate.

Malignant Tumors

Malignant tumors are divided into low grade tumors, high grade tumors, and tumor metastasis (independent of grade).

Stage I

Stage I (**low grade**) malignant tumors are further subdivided with regard to the containment into:

- **Stage IA**, i.e., the tumor remains inside the vertebra, and
- **Stage IB**, i.e., the tumor invades paravertebral compartments

No true capsule is associated with these lesions, but a thick pseudocapsule of reactive tissue often is penetrated by small, microscopic islands of tumor. Because resection along the pseudocapsule may leave behind residual foci of tumor, wide en bloc excision is indicated if possible.

Stage II

Stage II (**high grade**) malignant tumors are accordingly defined as:

- **Stage IIA**, i.e., the tumor remains inside the vertebra, and
- **Stage IIB**, i.e., the tumor invades paravertebral compartments

The neoplastic growth is so rapid that the host has no time to form a continuous reactive tissue layer. There is seeding with satellite tumor cells as well as skip lesions at some distance. These tumors show up on plain radiographs as radiolu-

cent and destructive lesions, often associated with pathological fractures. CT and MRI confirm the absence of a reactive tissue margin. Invasion of the epidural space is rapid particularly in Ewing's sarcoma or lymphoma, and is characterized by infiltrating tumor spread beyond the cortical border of the vertebra with no evident destruction. The resection should be wide or en bloc. The survival between Stages 1 and 3 differs significantly, whereas there is no difference in survival between patients with A or B lesions [3].

Stage III

In Stage III malignant tumors, metastasis represents the situation where the tumor has spread to a distant organ different from, and independent of, the histological grade of the primary tumor.

Non-operative Treatment

The treatment of spine tumors is determined by the:

- biology
- location
- extent of the lesion

For these reasons, establishing the tissue diagnosis is of great importance. It is extremely dangerous to wait and see if the biopsy is not reliable and the imaging studies not entirely conclusive.

The wait and see approach is rarely indicated

Even if the imaging findings indicate a benign lesion such as a vertebral hemangioma, the final histology may reveal a malignant lesion such as a solitary plasmocytoma [8]. For benign lesions, there are only rare indications for non-operative treatment, such as hemangioma or Langerhans cell histiocytosis. For malignant lesions, non-surgical treatment generally is an adjunct to surgery and consists of:

- pain management
- chemotherapy
- radiotherapy

Non-steroidal Anti-inflammatory Drugs

Non-steroidal anti-inflammatory drugs (NSAIDs) are often used for mild pain. Opioid drugs are used for severe pain. Other options include epidural and intrathecal administration of local anesthesia. Systemic steroids are used to control pain and mitigate neurologic deficit in patients with spinal cord compression. Chemotherapy has been valuable for the treatment of selected primary tumors and metastases such as osteosarcoma, Ewing's sarcoma and multiple myeloma. Radiotherapy has been the mainstay for treating radiosensitive primary malignant tumors such as Ewing's sarcoma as well as metastases [29].

Adjuvant Therapy

The goal of radiotherapy is to maximally destroy the tumor while minimizing the effects on normal tissue [10]. **Radiotherapy** may be the choice of initial treatment for radiosensitive lesions. With the advances in surgical technique and instrumentation, initial surgical excision followed by radiation if indicated is preferred because of the risk of developing postirradiation sarcoma. **Chemotherapy** is used particularly for the most common primary bone tumors such as osteosarcoma and Ewing's sarcoma. Its main effect is directed at reducing tumor volume and surrounding edema.

Radiotherapy is indicated for radiosensitive lesions

Chemotherapy is indicated particularly for osteosarcoma and Ewing's sarcoma

Operative Treatment

General Principles

The indication for operative treatment of spine tumors has to be carefully considered and treatment should be performed using a **team approach**. The biopsy path has to be carefully selected in order not to compromise further surgery. The type of resection depends on the synthesis of a plethora of parameters such as the biology of the tumor, the precise anatomic location, and the patient's general condition.

Traditionally, the indications for open surgery included:

- spinal instability due to bony destruction
- progressive neurologic deficit
- radioresistant tumor that is growing
- the need for open biopsy
- intractable pain unresponsive to non-surgical treatment

The primary goal is wide or en bloc resection and spinal reconstruction

Advances in vertebral resection and stabilization and improved survival with various neoadjuvant therapies have expanded the indications for surgical intervention of primary spinal tumors. Today, the ultimate goal must be a "**wide**" and preferably an **en bloc resection** of the primary tumor in combination with a spinal reconstruction which allows for early mobilization.

The **surgical techniques** are classified by the tissue planes and approach as:

- curettage
- intralesional resection
- en bloc resection

Curettage and **intralesional resection** describe a piecemeal removal of the tumor. **En bloc resection** indicates the attempt to remove the whole tumor in one piece together with a layer of normal tissue.

The resected pathological specimen is histologically analyzed, and further classified into:

- intralesional
- marginal
- wide

The term "**intralesional**" is used when the tumor mass is violated; **marginal** is appropriate when the surgeon dissects along the pseudocapsule, the layer of reactive tissue around the tumor; and "**wide**" is appropriate if surgical separation has occurred outside the pseudocapsule, removing the tumor with a continuous shell of healthy tissue.

It is essential to distinguish the removal en bloc, i.e., the whole tumor in one piece, from a simple intralesional procedure. Intralesional resection of malignant tumors may provide functional palliation and pain relief, but has a very high incidence of local recurrence [5]. When resecting a malignant spinal tumor, the

The widest possible margin should be sought for the excision of malignant spinal tumors

widest possible surgical margin should be sought. The goal of surgery should be complete extirpation of the tumor with stable reconstruction of the vertebral column. Resections involving extensively contaminated surgical margins or debulking should be avoided. An aggressive approach with adequate resection can enhance local control and prolong survival.

Surgical planning and decision-making are complex and require a team approach

Surgical planning and decision-making are complex processes. To address this difficulty, the vertebral elements are divided into zones [11, 27], thereby predicating the resectability of any particular lesion based on the zones involved [36, 43]. In the transverse plane, the vertebra is divided into 12 radiating zones (numbered 1–12 in clockwise order) and into five layers (A to E), starting from the
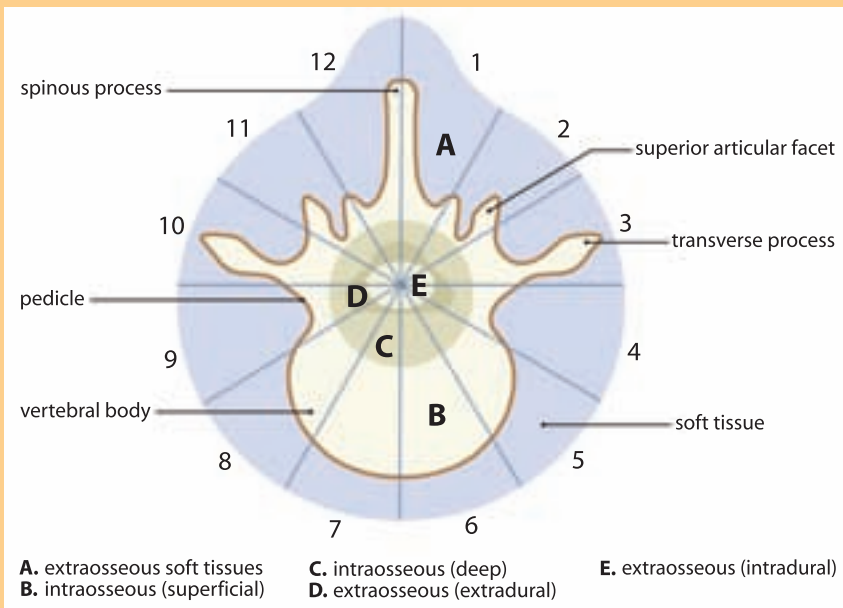
Figure 9. Surgical staging system

The transverse tumor extension is described with reference to 12 radiating zones and five concentric layers. (Redrawn and modified from Boriani et al. [11], reproduced with permission from Lippincott, Williams & Wilkins).

paravertebral osseous region to the dural involvement (**Fig. 9**). The longitudinal extent of the tumor is assessed by counting the spine segments involved. Comprehensive imaging studies are needed preoperatively to assess and describe the transverse and longitudinal expansion of a tumor, which allows appropriate surgical planning.

Surgical Techniques

The surgical techniques of primary spinal tumors are very complex and demand excellent surgical skills. Particularly for the en bloc resection of spinal tumors, the surgical strategy and reconstruction measure have to be decided on an individual basis because of a high variability of tumor location and extension. The surgeon should always consider that the final histological diagnosis may be different than expected or diagnosed on the biopsy material. Even in that case the surgeon should be capable of appropriately treating the case.

The final tumor diagnosis may be different than expected

A detailed description of the surgical techniques is far beyond the scope of this chapter. We prefer to concentrate on general principles rather than on a "how to do" approach. The surgery for primary malignant tumors should be concentrated in centers with sufficient case load and experience.

Consider referring primary spine tumors to a larger center

Intralesional Resection

This surgical technique is only used for benign tumors (**Case Introduction**) or for debulking of inoperable primary or metastatic lesions. The surgical approach for any malignant tumor of the spine is determined by the:

- tumor location
- extent of the tumor

The approach should be planned in such a manner as to provide the opportunity to excise the lesion completely as well as to stabilize the spine mechanically. Often, a combination of anterior and posterior approaches is used [12, 38]. In general, lesions involving the posterior elements of the spine with or without soft tissue extension are approached posteriorly for both resection and reconstruction (Case Study 2). If the lesion extends into the soft tissue, an appropriate soft tissue resection is required. In case of a typical osteoidosteoma, the lesion can be curetted and the bed of the tumor should be excised using a high-speed airdrill (Case Introduction).

If a malignant tumor involves the anterior vertebral body with or without soft tissue extension, but not the pedicle of the vertebral body or posterior elements, then an anterior approach is indicated. If a malignant lesion involves both anterior and posterior elements, an en bloc resection with a wide or even marginal resection is usually impossible unless the patient is willing to become paraplegic. The resection is usually accomplished by a combination of anterior and posterior approaches with intralesional contamination at the level of the pedicle when it is transected at the time of removal of the posterior elements [41]. In the thoracic and lumbar spine, some lesions involving both anterior and posterior elements are amenable to marginal resection through a posterolateral approach, thereby sacrificing a nerve root at the level of resection and one level above. The selected surgical approaches are chosen depending on the anatomic locations.

En Bloc Resection and Reconstruction of the Spine

There are three major methods of performing en bloc resections in the thoraco-lumbar spine:

- vertebrectomy
- sagittal resection
- resection of the posterior arch

The term "vertebrectomy," also termed "spondylectomy," is used to describe removal of the entire tumor in one piece together with portions of the posterior elements [37, 41, 43]. This approach is **indicated** if:

- tumor is confined to zones 4 – 8 or 5 – 9
- tumor is centrally located in the vertebral body
- at least one pedicle is free from tumor

The procedure can be performed in one or two stages. The posterior approach involves excision of the posterior elements, which allows the section of the anulus fibrosus and the posterior longitudinal ligament, careful hemostasis of the epidural venous plexus and posterior stabilization. The anterior approach, either by a transpleural thoracotomy, retroperitoneal, or thoracoabdominal approaches, allows the ligature of segmental vessels, proximal and distal discectomies, the en bloc removal of the vertebral body and anterior reconstruction [20, 38]. A bilateral approach for vertebrectomy has the main advantage of dissecting the tumor off the anterior soft-tissues under direct vision, thereby achieving a better margin.

When the tumor predominately involves the posterior spinal elements on one side (e.g., chondrosarcoma), an en bloc resection is feasible even in the presence of extensive soft tissue extension. In such cases, posterior serial pedicle and sagittal vertebral osteotomies in conjunction with rib resection are necessary (Case Study 3).

For **tumors of the sacrum** in particular, the surgical approach depends on the biology of the tumor as well as the anatomic location. The general principle is to remove the entire tumor mass in toto [4, 9, 28, 33]. It has been shown that for lesions below S3, a posterior approach only is sufficient whereas for lesions above
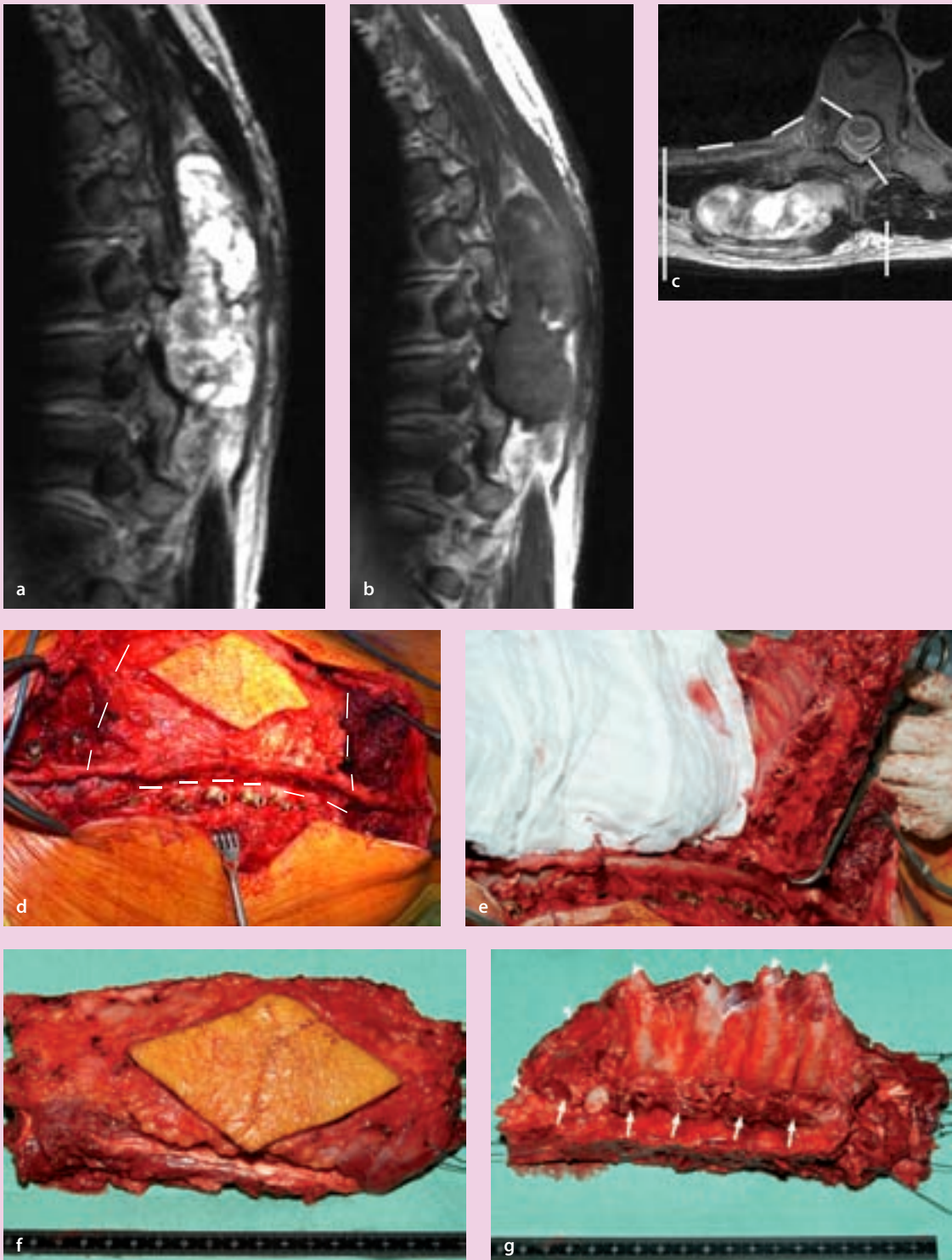
Case Study 3

A 50-year-old male presented with a painful parasagittal mass at the midthoracic spine. A diagnostic assessment included MRI, thoracoabdominal CT, bone scan and laboratory investigations. The T1W (a) and T2W MR (b) images showed a large polylobulated mass with varying signal intensity and a not clearly visible capsule. The tumor appeared to originate from the posterior part of the T7 pedicle (not shown). The soft tissue infiltration suggested a malignant

Case Study 3 (*Cont.*)

tumor. The axial T2W scans (**c**) demonstrated extension to the ribcage. A biopsy revealed the histological diagnosis of a Grade II chondrosarcoma. No metastases were discovered. An en bloc resection was planned. The lines indicate the level of osteotomies of the laminae, pedicles and ribs. The skin with the biopsy channel was excised (**d**). Prior to tumor resection, the spine was instrumented with pedicle screws at T3–T12 on the right side and at T3, T4, T11 and T12 on the left side. Tumor resection was performed along the indicated lines. The en bloc resection was done with serial contralateral laminotomies at T5–T10 (**e**), ipsilateral pedicle osteotomies at T5–T9, and rib osteotomies at T5–T10. An en bloc resection of the tumor was achieved with wide margins (**f**, **g**). Particularly the osteotomies at the level of the pedicles (*arrows*) and ribs (*arrowheads*) were tumor free. The resected pleura was covered with an artificial membrane (*asterisk*) and the dura with Gelfoam sponges (*arrowheads*). The spine was stabilized at T3–T12 and fusion was carried out on the right side (**h**). The defect was covered with an ipsilateral latissimus dorsi flap (**i**). Three years after surgery, the patient is functioning well although he had initial problems with the mobility of the left shoulder (unstable scapula). The follow-up radiographs show the stabilization of the spine at T3–T12 (**j**, **k**). Regular follow-up imaging studies (MRI, and thoracoabdominal CT scan) demonstrate a tumor-free course so far.

h

i

j

k
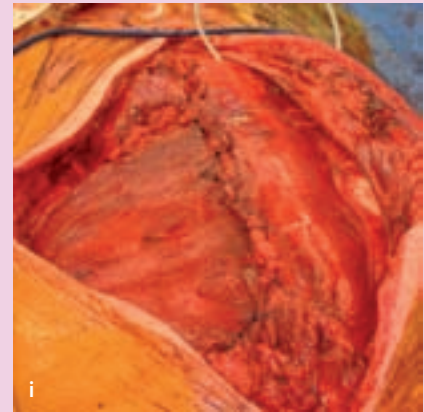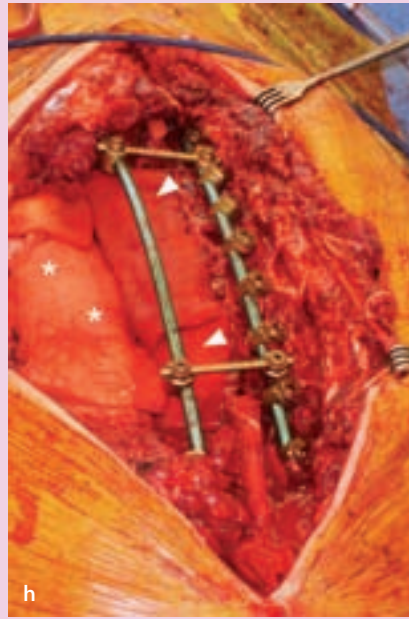
S3 a combined anterior and posterior approach is preferred [21]. The possible disadvantages of a posterior only approach include hemorrhage and laceration of pelvic viscera including ureters. The combined approach allows exposure of the entire pelvic contents and safe ligation of the internal iliac vessels, which assists in reducing bleeding during mobilization of the specimen from posteriorly. It has been shown that the combined approach reduces the local recurrence rate in patients with chordomas, and does not compromise the harvest and use of a pedicled transpelvic rectus flap for posterior wound closure [21].

Adjuvant Treatment and Local Recurrences

There are few large studies dealing with malignant primary bone tumors of the spine. Talac et al. [40] showed that local recurrence is directly related to the surgical margin obtained during surgery, with a fivefold increase comparing marginal and intralesional resections over wide resections. Because primary bone tumors are rare overall, in primary spine tumors in particular there are no randomized studies available which have assessed the outcome of combined treatment regimens. Basically, patients are treated, e.g., by chemotherapy according to the biology of the tumor independent of the location, including spinal locations. There are no large series which have assessed the effect of adjuvant treatment on the outcome of patients with primary malignant spine tumors. In a recent series, with the small numbers available, no conclusion could be drawn with respect to adjuvant treatment except for the fact that over 90% of patients who had local recurrences died from their disease.

The local recurrence is directly related to the surgical margin

Recapitulation

Epidemiology. Primary spine tumors are relatively rare. The **incidence** is estimated at 2.5–8.5 per 100000 individuals per year. When evaluating the potential of malignancy of a spine lesion, age of the patient and location of the lesion are the most important parameters.

Tumor biology. Cancer is a **molecular disease**. Cancer development is determined by the **five hallmarks of cancer**: unlimited replicative potential, avoidance of apoptosis, self-sufficient proliferation, angiogenesis and metastasis. **Metastasis** is the stepwise progression which includes proliferation, migration, invasion, intra- and extravasation, and local growth in the target organ.

Classification. Spine tumors are classified based on the **histological diagnosis**. Together with the age of the patient and the location of the lesion, the biology can be predicted, and treatment is performed accordingly.

Clinical presentation. Patients with spinal tumors present with pain, spinal deformity and neurologic deficit. **Back pain** is the most common symptom. It is persistent and usually not related to activity, and often aggravates during the night. Patients with spinal tumors **rarely** present with a **palpable mass**. Spinal instability and neurologic compromise may arise from a lesion in the vertebral body and depend on the level and location.

Diagnostic work-up. This includes laboratory investigations, imaging studies, and tumor staging with a biopsy from the lesion. Imaging studies include **standard radiographs** in two planes, **CT** and **MRI** as well as a **bone scan**. **Tumor staging** defines the systemic extent of the disease, which allows the prognosis to be determined, as well as the local extent, which is mandatory for surgical planning and should be done in accordance with the surgeon performing the tumor resection. The **biopsy** needs to be planned such that it does not compromise subsequent surgical resection. Serum calcium has to be evaluated, and anemia, hypoalbuminemia and electrolyte imbalances need to be assessed and corrected prior to surgery.

Treatment. Non-operative treatment is only indicated for benign lesions and if the patient is asymp-

tomatic. If surgery cannot be performed for malignant tumors, pain management is very important, and radiotherapy as well as chemotherapy needs to be taken into consideration. Surgical treatment can be performed as **curettage, intralesional** or **en bloc removal** of the tumor. Histologically, en bloc removal is classified into **wide**, **marginal** or **intralesional resection**. The goal of surgery is the complete extirpation of the tumor with stable reconstruction of the vertebral column. The surgical approach and technique is determined by the level and anatomic extent of the tumor lesion.

Key Articles

Hanahan D, Weinberg RA (2000) The hallmarks of cancer. Cell 100:57 – 70
Landmark paper on modern principles of carcinogenesis. This article describes the necessary key steps which a cell of a given tissue has to fulfill to become cancerous.

Sundaresan N, Boriani S, Rothman A, Holtzman R (2004) Tumours of the spine. J Neurooncology 69:273 – 290
This article provides a detailed overview of primary benign and malignant as well as metastatic bone tumors.

Fisher CG, Keynan O, Boyd MC, Dvorak MF (2005) The surgical management of primary tumors of the spine. Spine 30:1899 – 1908
This article underlines the importance of the surgical principles in the treatment of primary tumors of the spine.

Talac R, Yaszemki MJ, Currier BL, Fuchs B, Dekutoski MB, Kim CW, Sim FH (2002) Relationship between surgical margins and local recurrence in sarcomas of the spine. Clin Orthop Rel Res 397:127 – 132
This article comprises one of the largest and most recent series on the outcome of surgical treatment of primary bone sarcomas of the spine. It exemplifies the importance of obtaining a wide surgical margin.

Fuchs B, Dickey ID, Yaszemski MJ, Inwards CY, Sim FH (2005) Operative management of sacral chordoma. J Bone Joint Surg [Am] 87:2211 – 16
This article includes the largest series on surgically treated chordomas of the sacrum. It shows that for lesions above the S3 level, a combined anterior-posterior approach is preferred over a posterior approach alone.

Garg S, Dormans JP (2005) Tumors and tumor-like conditions of the spine in children. J Am Acad Orthop Surg 6:372 – 81
This article provides a comprehensive overview on tumors and tumor-like conditions in children. It highlights the differential diagnosis of back pain in children and adolescents and illustrates diagnostic and therapeutic options.

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