Spinal Cord Compression

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Abstract

Spinal cord compression, one of the most dreaded complications of malignancy, is usually caused by metastatic bone disease compressing the spinal cord and/or nerve roots. If not recognized and treated promptly, it can have potentially catastrophic outcomes. As patients live longer due to newer treatments, the incidence of malignant spinal cord compression may increase, and the types of presentation or behavior of tumors may change. Spinal cord compression must be considered in all patients who have a cancer diagnosis presenting with back or neck pain and/or neurological symptoms or signs. In this chapter, the terminology used in the diagnosis and treatment of spinal cord compression will be defined and the epidemiology and pathophysiology described. Given that spinal cord compression is a true emergency, it must be diagnosed and managed promptly by a multidisciplinary team. Early detection and effective treatment can make the difference between independent living and being bed bound. This chapter will explore the many factors that should be considered in determining the most appropriate care plan and highlight how the ultimate goals of care and care plan need to be continually reassessed to ensure the best outcome for the patient. Surgical intervention and radiotherapy treatment decisions are complex and will be explained in detail, within the context of these above considerations. Technical aspects and illustrations to clarify treatment options will be provided. Predicted outcomes will be discussed; however it is important to note that the best outcomes occur when the degree of premorbid neurological deficit is minimal and the diagnosis and treatment initiated within 24–48 h of presentation.

1 Introduction

Spinal cord compression is one of the most dreaded complications of malignancy usually caused by metastatic bone disease compressing the spinal cord and/or nerve roots, with potentially catastrophic outcomes. It affects up to 14% of patients with cancer and is a true emergency, which must be diagnosed and managed promptly by a multidisciplinary team, taking into account many factors to instigate the most appropriate care plan for that individual patient. Best outcomes occur when the degree of premorbid neurological deficit is minimal and the diagnosis and treatment initiated within 24–48 h of presentation.

2 Definitions

Within this chapter, it is necessary to define the common interpretation of the terms used. The term "spinal cord compression" in degenerative terms is just that; compression of the spinal cord alone by a structure such as bone or disc. In malignant parlance, it has a much broader definition, and it usually refers to compression of the spinal cord or cauda equina either directly from a malignancy or compression by a pathological fracture caused by a malignancy and its associated clinical findings. Malignant spinal cord compression also commonly involves the compression of nerve roots in the intervertebral foramina and is an integral part of the clinical picture in the symptom pattern (Fig. 1) (Cole and Patchell 2008).

It is best to maintain strict clinical and radiological definitions. "Malignant spinal cord compression" should only include compression of the spinal cord and conus, whereas "malignant cauda equina compression" is the compression of the lumbar nerve roots in the lumbar vertebral canal. "Malignant nerve root compression" is the involvement of the nerve roots, including within the intervertebral foramina. It is important to distinguish between the use of the term compression in relation to clinical syndromes. Compression is the mechanical compression of the spinal cord or nerve roots as defined radiologically. Therefore cauda equina compression is a radiological definition and should not be confused with "cauda equina syndrome," which is the clinical picture of nerve root signs, perianal sensory loss, and double incontinence. It is important to remember that a patient can have radiological compression without symptoms. This is termed "subclinical cord compression."

"Impending cord compression" is a loose term that should be avoided. It is used frequently to indicate a radiological finding that may progress to definite cord compression, either from tumor growth or bone fracture. Instead the term "at risk of spinal cord compression" should be used.

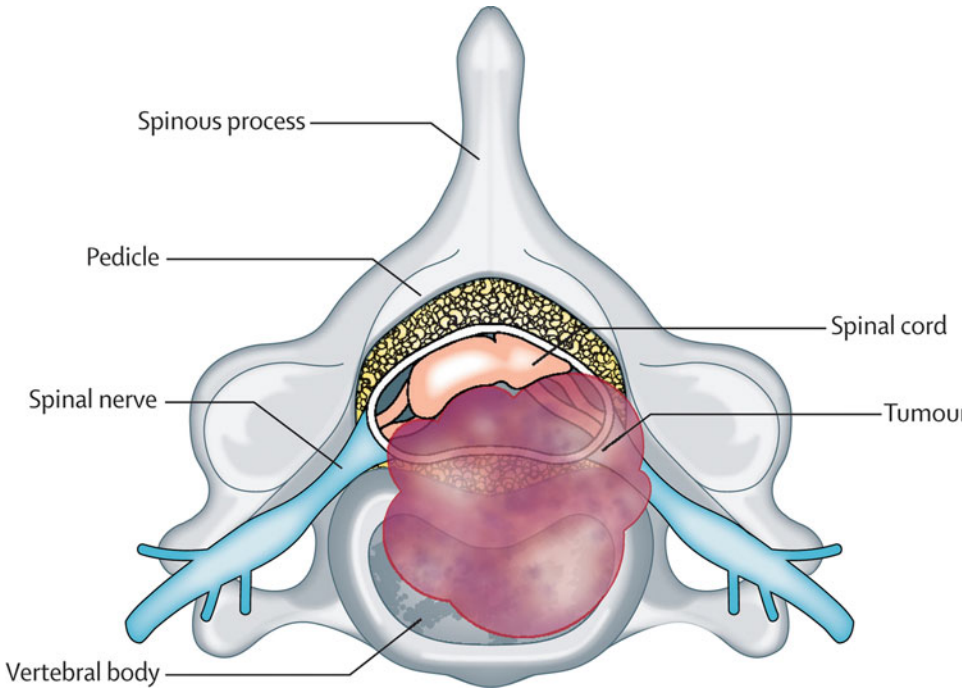

Fig. 1 Example of a tumor within a vertebral body, anterior to the spinal cord which is growing posteriorly into the vertebral canal to compress the spinal cord and/or nerve roots

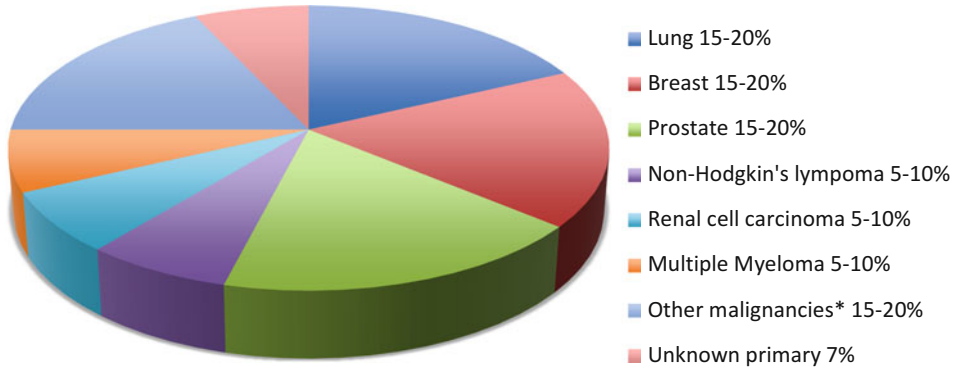

Fig. 2 Approximate proportion of primary tumors causing malignant spinal cord compression. *Other malignancies include colorectal carcinomas, sarcomas, melanomas, etc.

"Unstable fracture" in relation to malignancy indicates a vertebra that has developed a fracture and may possibly collapse further from loss of supportive elements. A "potentially unstable vertebra" is one that has lost a significant amount of its supportive elements and may go on to fracture.

3 Epidemiology and Pathophysiology

Estimates of the incidence of spinal cord compression from malignancy are variously quoted as between 5% and 14% of people with cancer (National Institute for Health and Clinical Excellence (NICE) 2008). In patients with bone metastases, approximately 60% will have metastases within the spine, and up to 10% of these patients will develop spinal cord compression (Spratt et al. 2017). With new treatments, patients with cancer are living longer, and it is likely that the incidence of spinal cord compression may increase. Of patients presenting with spinal cord compression, 77% have a known pre-existing malignancy. The remaining 23% have spinal cord compression as their first presentation of their malignancy (Levack et al. 2002).

Lung, breast, and prostate cancers are the commonest malignancies causing spinal cord compression and together account for over 50% of cases. Non-Hodgkin's lymphoma, renal cell cancer, and multiple myeloma each account for 5–10%, and most of the remainder of cases of malignant spinal cord compression are due to colorectal cancers, sarcomas, and melanomas (Cole and Patchell 2008). In 7% of patients, the site of primary tumor may remain unidentified (Fig. 2) (Levack et al. 2002).

The thoracic spine is most commonly affected with up to 70% of lesions. About 30% of lesions are within the lumbosacral spine and under 10% within the cervical spine (Helwig-Larsen and Sorensen 1994) (Fig. 3). Seventeen percent of patients have two or more levels of spinal cord compression (Levack et al. 2002).

Spinal cord and cauda equina compression can result from several different mechanisms. Direct growth of tumor (either from a vertebra or from paraspinal tissues) into the vertebral canal or intervertebral foramina is one mechanism. A pathological fracture with displacement of bone fragments is another. Often it is a combination of both. Malignant cells within the subarachnoid space may also result in neurological deficits caused by tumor deposits growing on the nerves or surface of the spinal cord within the vertebral canal. From a clinical perspective, it is helpful to consider any tumor in the subdural and subarachnoid space or within the spinal cord itself (compromising the spinal cord) as a cause of a patient's symptoms and signs and as lesions where a patient may benefit from treatment. Leptomeningeal disease is most commonly seen in patients with small cell lung cancer, melanoma, lymphoma, and tumors of the central nervous system, most commonly medulloblastoma.

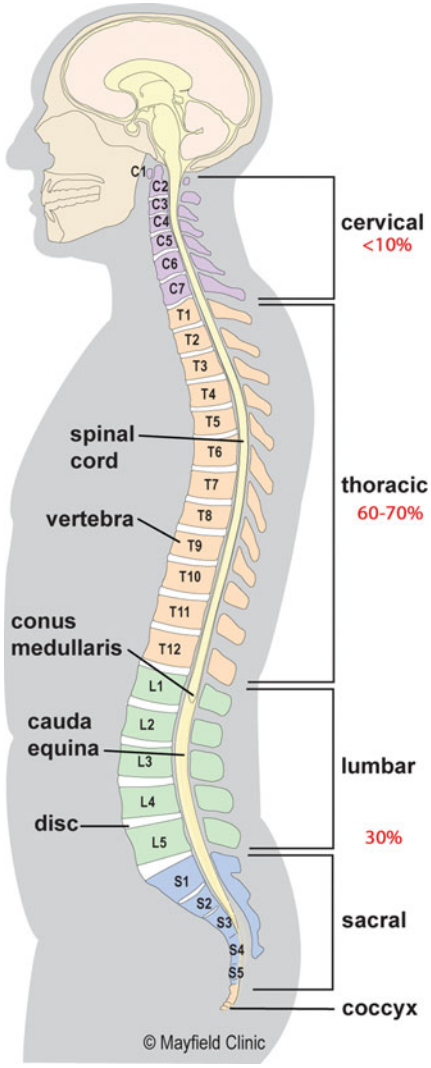

Fig. 3 Approximate distribution of the location of malignant spinal cord compression presentations. Percentages are given in red. 17% of patients have two or more levels of cord compression. (Illustration by Martha Headworth, printed with permission © 2016 Mayfield Clinic)

4 Clinical Features

Malignant spinal cord compression is one of the most dreaded complications of metastatic cancer. Its natural history, if untreated, is usually one of relentless and progressive pain, paralysis, sensory loss, and sphincter dysfunction (Loblaw and Perry 2005). These symptoms and signs can vary significantly between patients (Fig. 4), and therefore a detailed history and full neurological examination need to be performed and documented.

Back pain, the most common presenting problem in patients with spinal cord compression, may be sharp, shooting, deep, or burning. The pain can be localized to the back or may radiate in a band-like dermatomal distribution, if tumor compresses the nerve roots in or near the intervertebral foramina. Mechanical back pain is important to recognize, as it can be associated with spinal instability. An acute exacerbation of chronic back pain may be caused by a recent compression fracture.

In addition to pain, other common symptoms of spinal cord compression include motor dysfunction (weakness with associated reduction in mobility and/or sphincter disturbance with incontinence), sensory changes (paresthesia and loss of sensation), and autonomic dysfunction (urinary hesitancy and retention). At presentation patients tend to be more paraparetic than paralyzed and tend to be less aware of the sensory changes. Sphincter disturbance is usually a poor prognostic sign with regard to preservation or improvement of ambulatory status.

Patients with cauda equina syndrome usually present differently, with change in or loss of sensation over the buttock region, posterior-superior thighs, and perineal region. This is described as a "saddle distribution." Reduced anal tone and urinary retention, with overflow incontinence, are typically present.

A study (Husband 1998) of patients with malignant spinal cord compression found that more than half of the patients had lost further neurological function between the onset of symptoms and start of treatment. The majority of delays were attributed to lack of symptom recognition by the patient and diagnostic delay by the primary health provider or at the general hospital.

To prevent further deterioration and maximize the chances of neurological recovery, any new back pain or abnormal neurology that develops in a patient with a known malignancy needs to be investigated immediately, as the diagnosis of spinal cord compression warrants strong consideration.

Clinical symptom	Incidence in patients with spinal cord compression	Features
Back pain	83-95%	Localised or radicular Unilateral or bilateral Often worse at night Can be mechanical (worse with movement)
Motor deficits & difficulty ambulating	35-75%	Often described as 'heaviness or clumsiness' by patient Weakness on examination Can involve upper or lower motor neuron signs depending on level involved
Sensory deficts	50-70%	Change/loss of sensation typically begins distally and ascends as the disease advances
Autonomic dysfunction	50-60%	Bowel or bladder symptoms tend to occur late Rarely a presenting symtom

Fig. 4 Summary of the different clinical presentations of patients with malignant spinal cord compression (Cole and Patchell 2008)

Several studies have shown that patients with the slowest development of motor deficits before treatment had the best functional outcome compared with patients with faster development of motor deficits and that a greater interval from cancer diagnosis to the spinal cord compression independently predicted improved survival (Rades et al. 2002). Each of these factors probably reflects the presence of less aggressive tumors. Subclinical spinal cord compression (radiological evidence of cord compression in the absence of neurological deficits or pain) is also important to recognize as it represents a window for treatment with potentially the best clinical outcomes.

5 Radiological Diagnosis

5.1 Referral to Radiology

A low index of suspicion in a patient with a known malignancy is important. In a patient with the new onset of a neurological deficit, including bowel and bladder dysfunction or limb weakness, where malignant spinal cord compression or cauda equina syndrome is suspected, same-day magnetic resonance imaging (MRI) is important if the patient is deemed fit for treatment and this will be carried out in the same time frame. If a patient is not fit for treatment or would refuse any treatments offered, there is a little benefit in putting the patient through an MRI scan. The MRI scan can take up to an hour and can be an unpleasant experience for a patient, especially one who is in pain. Therefore if an MRI scan will not alter management, consider not referring the patient.

As a suspected spinal cord or cauda equina compression in a patient who is fit for treatment is a medical emergency, a personal phone call to the radiologist to expedite the radiological investigation is helpful. Discussion of the patient's underlying malignancy, symptoms, and signs assists the radiologist in determining the most appropriate imaging techniques and dedicated sequences, including extra sequences through the area of the spine that could be responsible for

the neurological abnormality, to answer the clinical question and to look for other causes of the patient's presentation. It is critical to good radiological investigation that the patient is examined thoroughly. While imaging should include the whole spine, a radiologist who is aware of the neurological findings may detect smaller lesions on the extra, dedicated sequences that would not necessarily be seen on standard sequences.

The referral (or request) should include information about:

- Nature of the known malignancy
- Neurological findings
- Allergies
- Renal function
- Contraindications to MRI (detailed below)

5.2 Patient Care and Optimization of Image Quality

These patients are often in pain and usually anxious. The MRI scanner table is hard and uncomfortable. An examination of the whole spine can take 1 h, and it is imperative that the patient does not move during the examination. Some MRI sequences can take over 8 min, and any movement during this time can result in non-diagnostic images. It is helpful for patients to understand what to expect: radiographers are good at explaining the technical side of MRI to patients but do not have the training or knowledge of the clinical situation to be able to provide a more holistic explanation. For patient comfort and better diagnostic results, it is helpful for patients to be prescribed an appropriate dose of a suitable analgesic prior to the scan, such as morphine. This should be administered when the radiographers call the ward to arrange transport of the patient to MRI.

5.3 Radiological Techniques

Magnetic resonance imaging (MRI) is the imaging technique of choice (Baur et al. 2002; Jung et al. 2003) (Figs. 5, 6, and 7). Its advantages include:

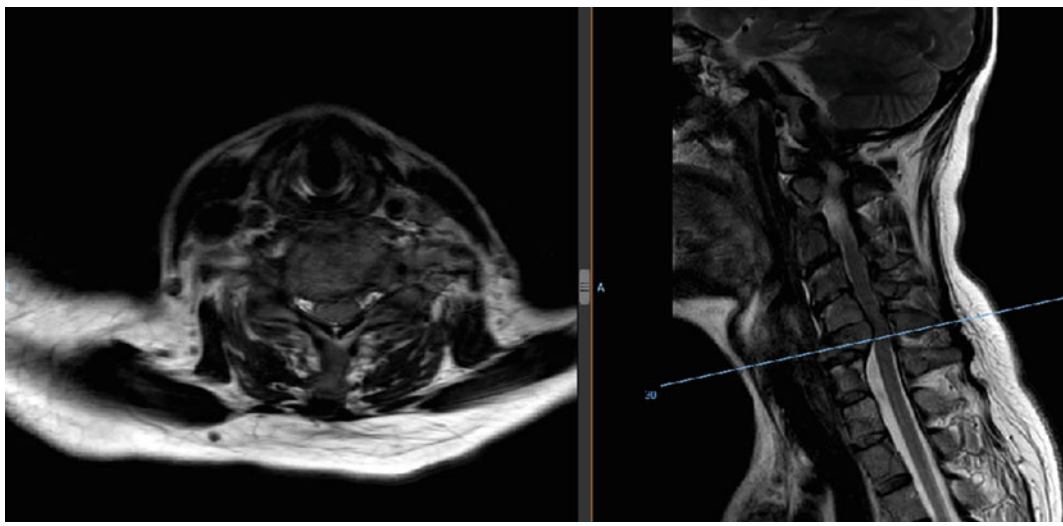

Fig. 5 A 50-year-old female with metastatic breast cancer to the bone only presented with neck pain/tenderness, increased upper limb reflexes, and urinary incontinence. Tenderness over the T5 level with associated bilateral radiating pain was also noted. An axial T2-weighted MR image (on left) through the C6 vertebra and a sagittal T2-weighted MR image of the cervical spine and upper thoracic spine (on right, with blue line demonstrating the level of the corresponding axial image). Confluent tumor at C5 and C6 levels replaces the vertebral bodies, with extension posteriorly into the vertebral canal, resulting in spinal cord compression. The signal return from the spinal cord is within normal limits

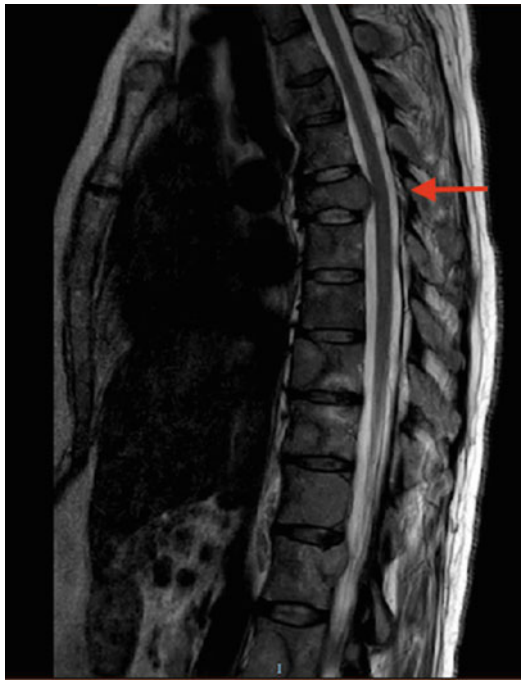

Fig. 6 A T2-weighted sagittal image of the thoracic spine of the same patient demonstrating a lesion in the T5 vertebral body extending into the anterior extradural space and abutting the ventral surface of the spinal cord (red arrow), without signal change within the cord. Numerous metastases involving the entire vertebral column were found on the whole spine images

- The ability to obtain images in any plane: usually at least two perpendicular planes and often three planes
- Good contrast between the relevant tissues including the spinal cord, nerve roots, cerebrospinal fluid, vertebrae, surrounding tissues, and tumor
- Good spatial resolution when the appropriate sequences are obtained and the patient is able to stay very still

There are, however, some disadvantages of MRI. These include:

- A long time required to acquire the imaging
- Patient discomfort if not adequately managed in advance
- Lack of access to MRI, especially for patients in rural locations or in departments where the MRI scanner is heavily booked (there are few opportunities to add in an extra patient with potential spinal cord compression, not least because of the long scanning time required for a full spine MRI)
- Difficulty monitoring patients when in the MRI scanner

MRI has a number of *absolute* contraindications. These include:

- Pacemakers: There are now some pacemakers that are MRI-compatible, but the majority are potentially lethal and without firm evidence of MRI compatibility; a pacemaker is an absolute contraindication.
- Defibrillators and other implanted stimulators.
- Aneurysm clips: The clips currently used by neurosurgeons are MRI-compatible, but many older clips are not. Placing a patient with an incompatible aneurysm clip in the MRI scanner can result in the clip twisting and tearing off the artery with fatal consequences. Unless there is definite proof that the clip type is safe, a patient with an aneurysm clip cannot be placed in the MRI scanner.
- Metal in the eye: Those who weld and grind metal can get metal fragments in the eye. If these have not been removed, then it is not safe to place the patient in the MRI scanner as the metal fragment may move, causing blindness.
- Some heart valves and intravascular stents are absolute contraindications. Definite proof of the nature of MRI-compatible devices is required prior to a patient being allowed in the MRI scanner.

Relative contraindications include:

- Being confused and/or unable to follow instructions. Communication problems can pose a risk with safety screening and an inability to understand the need to stay still for sufficient time to get diagnostic-quality images.
- Claustrophobia can result in a patient being unable to stay still in the MRI scanner or to stay in the scanner at all. Premedication with an anxiolytic can be helpful. The same effect may

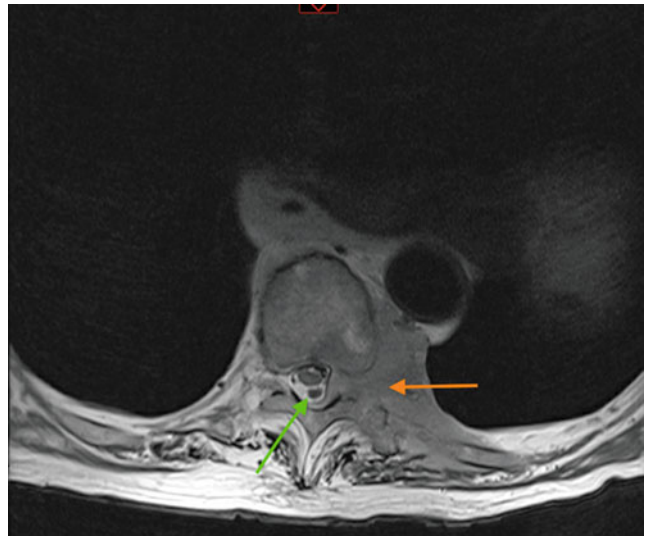

Fig. 7 This 93-year-old patient had metastatic angiosarcoma and presented with mid-lower thoracic radicular pain, radiating in a left T9–T10 dermatomal distribution. An axial T2-weighted MR image of the patient through the T9 level. There is nerve root compression from a left-sided paravertebral mass extending into the vertebral canal through the intervertebral foramen. The spinal cord is displaced to the right. Signal return within the spinal cord is normal (Orange arrow: tumor in the intervertebral foramen. Green arrow: tumor in the vertebral canal)

also be achieved by adequate analgesia with opiates.

- Recent operations with metal implants or clips. These items are problematic with recent operations (due to potential movement) and are considered safe after 6 weeks. Although it is safe to perform MRI after this period, as the prosthesis is fixed and stable, local tissue heating can occur. Patients are asked to let the radiographer know if they start to feel an area of heat. Metal in tattoo pigments can cause a similar effect.
- There is long checklist of other potential contraindications about which the radiographer and radiologist will need to be aware. The radiographer will complete this before an MRI scan can be performed. If the patient cannot speak English (or the language spoken in the country where he or she is being treated), an interpreter will be needed to complete the safety checklist.

If a patient is unable to undergo an MRI scan, then a CT scan and CT myelogram are appropriate imaging techniques. CT myelography is preferred as this more clearly demonstrates the effect of vertebral metastases on the spinal cord and intrathecal nerve roots. This is particularly helpful in the cervical and thoracic spine where a combination of artifacts from surrounding structures and little CSF surrounding the spinal cord can make it technically challenging to interpret a standard CT scan of the spine. Imaging patients with cauda equina syndrome can often be achieved with a CT scan alone. Myelography without a CT scan is no longer the standard of care. The lack of spatial and contrast resolution compromises clinical decision-making. On occasion a CT scan may assist a spine surgeon in planning treatment due to the better delineation of bony structures when compared with MRI. In this instance, the CT scan should be restricted to the region being treated.

The radiology report should always include a description of the extent and location of metastases, the effect (if any) on the spinal cord and nerve roots, any deformities of the spine, and any disease noted in adjacent tissues.

6 Goals of Treatment

The management options and decisions involved are complex for the team treating patients with malignant spinal cord compression. Perhaps the most fundamental question that must first be answered is as follows: *What are the goals of treatment*? The next question that follows is: *Are these goals actually achievable*? For example, the ultimate goal might be to regain the ability to walk, but the achievable goal may be to retain bed mobility and improve the patient's pain levels to enable easier transfers (from bed to chair). These treatment goals should be revisited at each decision point during a patient's management, ensuring that futile treatment is not recommended, and the "bigger picture" is kept in mind. Patients, their carers, and treating teams need to be open and honest about treatment goals.

To answer these questions relating to treatment goals, the key factors to consider are mobility, continence, analgesia, estimated prognosis of the patient, and patient preferences. Active treatments should be explored if ambulatory or sphincter function can be potentially preserved or recovered, or pain levels improved. These treatments include surgical interventions and/or radiotherapy. Best supportive care is imperative for all patients. The overarching treatment aim is always to improve the patient's quality of life.

7 Management Overview and Decision Process

Prompt diagnosis and instigation of appropriate treatment strongly affect the patient's ultimate outcome. The strongest prognostic factor for overall survival and the ability to ambulate after treatment is pretreatment neurological status and specifically motor function (Talcott et al. 1999). Therefore in a patient with known cancer, new back pain or abnormal neurological symptoms or signs should be investigated immediately. If the diagnosis of spinal cord compression is not consistent with the patient's known cancer biology, consideration should be given to arranging a biopsy. This will assist in excluding differential diagnoses, such as osteomyelitis.

Once the diagnosis of malignant spinal cord compression is confirmed, the treatment decisions need to be made quickly by the multidisciplinary team, comprising of the neurosurgeon, oncologists (both radiation and medical), palliative care physician, and community teams including the primary care provider. Urgent neurosurgical opinion should be considered for patients with symptomatic spinal cord compression, as evidence suggests that in selected patients, outcomes are better with decompressive surgery prior to radiotherapy (Patchell et al. 2005). Several national treatment guidelines and protocols suggest that treatment with surgery or radiotherapy ideally should be commenced within 24 h of *radiological diagnosis* for best functional outcome (National Institute for Health and Care Excellence (NICE) 2014; eviQ Cancer Treatments Online (Cancer Institute NSW) 2012), together with other studies confirming better outcomes if surgery is performed within 48 h of *initial presentation of symptoms* (Quraishi et al. 2013).

This initial multidisciplinary decision process may be performed utilizing a "virtual consultation" via telephone or the Internet, especially if the neurosurgical and oncology specialists are geographically distant from the patient. The treatment options can be divided into four categories (surgery, radiotherapy, systemic and supportive care) and will be detailed further in the next sections. Most patients require a combination of these treatments; however the decisions regarding sequencing can be complex.

There are many factors that the multidisciplinary team considers in developing a suitable treatment plan for each patient with malignant spinal cord compression. These can be divided into patient, tumor, and treatment factors (Fig. 8).

All of these factors are then synthesized together to choose the most appropriate treatment recommendation. For instance, for a patient with surgically appropriate disease, who has never received radiotherapy to the spine, with minimal burden of disease, and an excellent expected long-term prognosis, both surgical management and adjuvant radiotherapy would be recommended,

PATIENT FACTORS	Functional impact of symptoms (mobility & continence) Performance status (often measured as EGOG status) (Oken M 1982) prior to onset of syptoms/signs Pain levels Patient preferences Time elapsed since developing symptoms/signs Physical location of patient (distance to travel to hospital for surgery &/or radiotherapy delivery)) Any improvement with dexamethasone
TUMOUR FACTORS	Structural impact of disease (e.g. presence of bony compression and spinal instability) Levels within the spine involved Estimated prognosis • Bone only +/- visceral metastases • True 'oligo-metastatic' disease • Underlying cancer biology/progression
TREATMENT FACTORS	Predicted outcome from active treatments (i.e. potentially reverse or preserve function, or improve pain) Estimated length of time to achieve potential benefit from treatments Technical surgical factors Radio-responsiveness of tumour Response to systemic treatment options Previous treatments (neurosurgical interventions and radiotherapy in particular) Toxicities expected from treatments

Fig. 8 Factors to be considered by the multidisciplinary team in formulating a care plan for patients with malignant spinal cord compression

in addition to exploring aggressive systemic treatment with the best supportive care. For a patient with a poor performance status, previously treated spinal cord compression, who has a short prognosis and has exhausted systemic options, further surgery and/or radiotherapy may not be able to provide any potential benefit, and instead best supportive care alone is probably the best option. These factors will be explored further in the following section with respect to each treatment intervention, but it is important to further elaborate on a few general factors.

Given that the overall aim is to improve the patient's quality of life, it is extremely important to consider the premorbid level of function of the patient and what improvements are achievable. At best, interventions are able to reverse neurological abnormalities back to the patient's baseline level and eradicate pain. In practice this can be difficult to achieve, and therefore an honest and accurate estimation of "possible" versus "likely" benefit needs to be discussed with the patient and carers. Pain can be temporarily improved with steroid medication and analgesia, together with pressure care, insertion of indwelling urinary catheters, and other important supportive care measures. For more durable analgesia benefit, surgery and/or radiotherapy are the best options.

Estimated overall disease prognosis can be very difficult to predict accurately, despite many tools being developed (Krishnan et al. 2013), and probably deserves its own separate chapter. Essentially, if a patient has had a long disease-free interval (from diagnosis or last episode of disease progression to the development of spinal cord compression), has promising systemic options, or has oligo-metastatic disease, then they are likely to have a longer prognosis. Patients with particular tumor biologies (e.g., metastatic prostate cancer or receptor-positive breast cancer with bone-only disease) may also have better prognoses. The oncologist and palliative care physician who know the patient most closely are best placed to make this prognosis estimation.

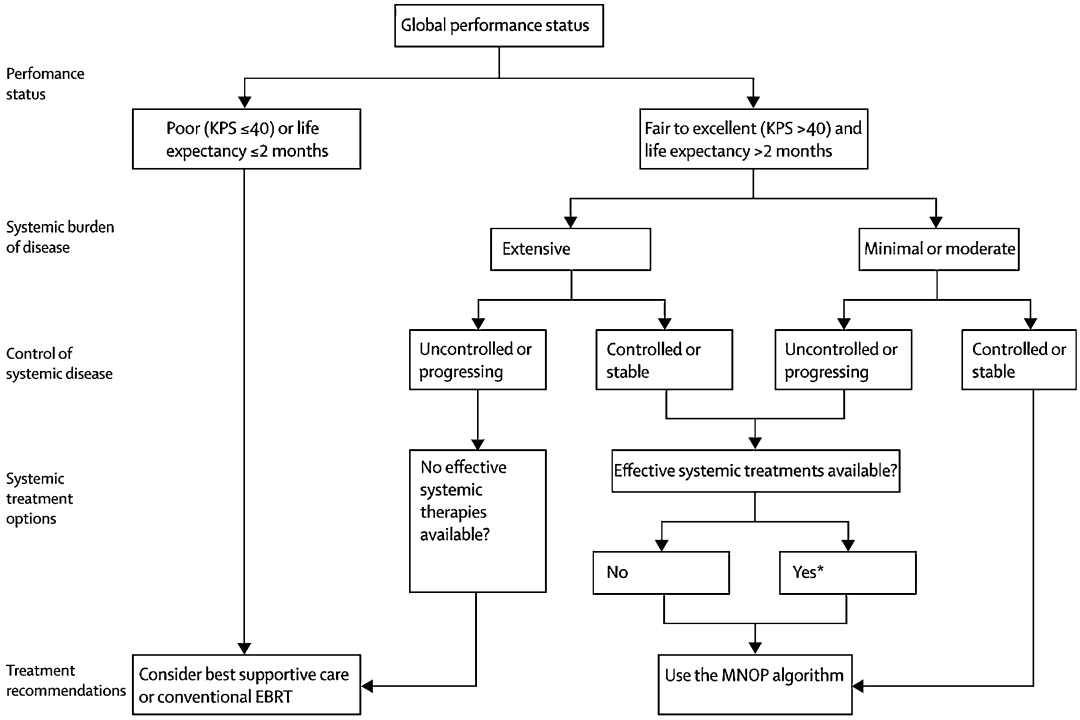

Fig. 9 Algorithm 1: initial assessment algorithm for patients with spinal metastases. *KPS* Karnofsky Performance status, *EBRT* external beam radiotherapy, *MNOP* mechanical, neurological, oncological, preferred treatment. *For selected patients with effective systemic therapy treatment options, systemic therapy without the use of radiotherapy might be most appropriate

For surgery and/or radiotherapy to achieve potential overall benefit, the predicted prognosis must be long enough to allow these treatments to be delivered, the toxicities managed, the patient to recover, and the best possible treatment outcomes realized. In the case of combined surgery and radiotherapy, a good rule of thumb is that if overall prognosis is less than 3 months, the patient may not live long enough to recover from the operation and anesthetic, proceed to radiotherapy (often five daily treatments over 1 week), heal from side effects, and await the 4–6 weeks it usually takes for maximal analgesia response and the initial consolidation of the structural benefit from radiotherapy. This has to be balanced by the patient's wishes and acceptance of potentially spending a prolonged period of time either in hospital or away from their usual place of residence, to receive these treatments.

Essentially the long-term benefits of an invasive, timely, or costly procedure might not manifest in patients with a short life expectancy. Furthermore, an overly aggressive treatment approach might cause more harm than benefit in patients who are frail and neurologically debilitated, or who are dying (Spratt et al. 2017). A number of algorithms have been developed to assist management teams in deciding appropriate treatment. The recent Lancet oncology review by Spratt et al. summarizes one such approach in patients with spinal metastases (Figs. 9 and 10) (Spratt et al. 2017). Spinal cord compression is detailed in the far-right portion (red box) of the MNOP (mechanical, neurological, oncological, preferred treatment) algorithm (Fig. 10).

8 Neurosurgical Intervention Overview

Surgical treatment in the management of malignant spinal cord or cauda equina compression remains controversial and difficult. It is not always an available option. The commonest treatment options are decompression, stabilization, or

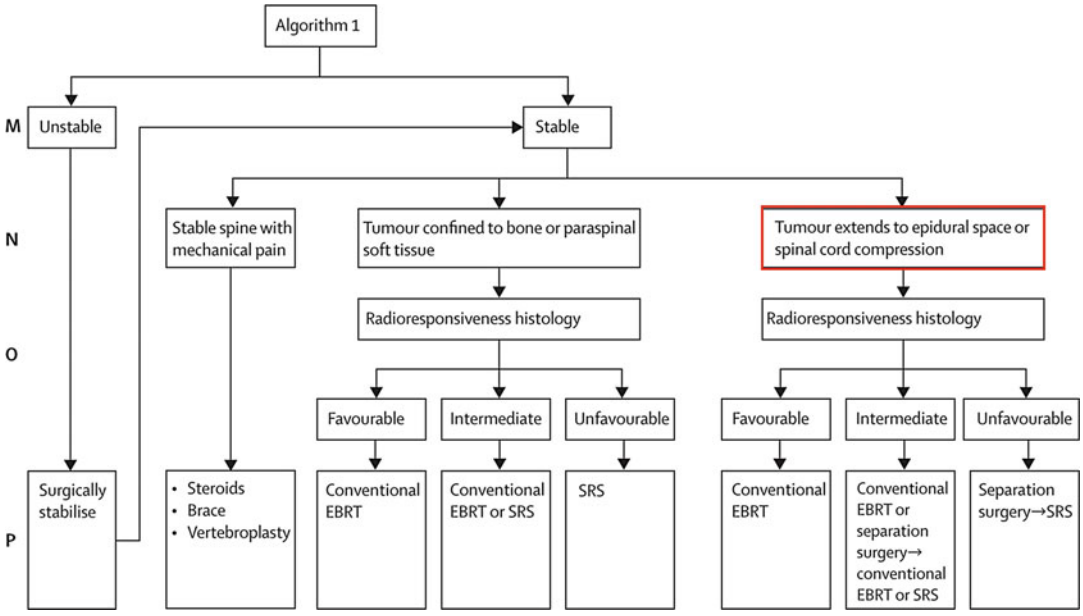

Fig. 10 MNOP algorithm for management of spinal metastases. Spinal cord compression is detailed in the far-right portion (red box). *MNOP* mechanical, neurological, oncological, preferred treatment, *EBRT* external beam radiotherapy, *SRS* stereotactic radiosurgery

both. The best-known studies showed that decompression alone produced a similar or worse outcome when compared with radiotherapy alone for malignant spinal cord compression, due to the destabilizing influence of the operation (George et al. 2015). For this reason, the majority of patients who now have surgery for spinal cord compression will have decompression combined with a form of stabilization. The preferred option is to make the decision and enact it, *prior* to the onset of major symptoms and signs. Prolonged paraplegia in a patient from malignant compression will generally not resolve with surgery.

The typical goals of surgery are:

1. Prevention of neurological deterioration
2. Restoration of neurological function
3. Treatment of pain from compression
4. Fracture stabilization for pain control and prevention of progressive deformity

The decision to operate needs to be based on the assessment of the value to the patient from the procedure. The questions that need to be asked are:

What does the patient want?

Patients will usually have an opinion in regard to what they are prepared to go through. This will depend on their expectations of the outcome. The potential outcomes must not be overstated. Surgery is going to be associated with a period of convalescence and likely rehabilitation, and the patient may not want to go through this.

Is surgery technically possible and what are the risks?

A surgical opinion with review of the radiology prior to discussion with the patient is invaluable, as many patients are not technically suitable for surgical intervention or the procedure will be too large considering the patient's condition.

Is the patient fit for any operation planned?

Surgery is precluded if the patient cannot have a prolonged anesthetic, is unable to stop any blood thinner medications, or is neutropenic or thrombocytopenic.

Is there a significant benefit to the patient from the surgery?

If the patient cannot walk prior to the surgery and has a predicted survival of less than 3 months, they are unlikely to walk again. If a patient has severe pain and has an unstable crush fracture, then stabilization should reduce the pain substantially which will significantly decrease medication requirements and hopefully supportive care measures, thereby improving quality of life.

What is the patient's life expectancy?

The only surgery that should be entertained in patients with short life expectancy is for the treatment of pain. If there is a long life expectancy, then it is appropriate to consider treatment early, as prevention of fractures and subsequent pain, kyphosis, and neurological deficit is ideal.

Rate of growth of the tumor and alternative treatment options?

In the palliative treatment of metastatic cancer involving the spine, it must be remembered that surgery is a temporary option, as the tumor will recur. If the lesion is radioresistant and there are no medical options, then even with surgical treatment, there is likely to be residual disease, and hence regrowth will occur at the known existing disease progression rate.

Should radiotherapy/radiosurgery be used perioperatively?

Conventional radiotherapy will affect tissue healing. If the patient has already had radiotherapy and subsequent surgery is planned, postoperative wound breakdown and infection will be much more likely. If stereotactic surgery to the tumor bed is planned, insertion of metal hardware may cause scatter of the radiation and affect the ability to plan the radiotherapy accurately. Preoperative radiosurgery, if time permits, may be a better and simpler option. If postoperative radiotherapy is planned, a period of at least 2 weeks is usually required for surgical healing, prior to fractionated radiotherapy.

9 Neurosurgical Procedures

9.1 Laminectomy

This involves the removal of a lamina from the back of the spine, thereby exposing the vertebral canal and allowing access to the spinal cord and any tumor around it. This is only suitable for patients who do not have any instability and predominately posterior and lateral extradural compression.

9.2 Stabilization Alone

This is usually a posterior procedure in the thoracic and lumbar spine. It involves the insertion of screws into the pedicles of the vertebral bodies and the linking of the screws to a rod that will cross an unstable segment of fracture. It can be imagined as an internal fixture or scaffolding. These are now usually constructed from titanium and, if done without other procedures, will be performed by a minimally invasive or percutaneous technique. Stabilization can be used in combination with external beam or stereotactic radiotherapy where tumor control would be adequate with radiation alone, but there is a risk of vertebral collapse.

9.3 Laminectomy with Posterior Stabilization

This is a combination of the above two procedures and allows for a more extensive bone removal and hence a wider decompression. In this combined procedure, the decompression may extend to involve the pedicles and part of the vertebra, which may then cause instability that needs to be treated with the stabilization. It may be a completely open procedure or combined with a minimally invasive technique.

9.4 Vertebrectomy with Stabilization

If the vertebra needs to be removed, this usually involves an anterior approach, but some surgeons will do certain levels from a posterior approach. The complexity and size of the operation increases from less complex in the cervical spine to much more complex in the lumbar spine. At most levels in the cervical spine, vertebrectomy with stabilization is relatively uncomplicated. Anterior surgery at vertebral levels C1 and C2 is not indicated in the palliative setting because of its complexity and risks. Similarly anterior surgery at vertebral levels T3–T5 is best avoided in the palliative setting. These levels are best treated from behind. If there is a high degree of instability either from the tumor or the operation, then an anterior decompression will be combined with posterior stabilization. Anterior surgical procedures in the lumbar and thoracic spine are less likely to be entertained in the palliative setting because of the risks.

10 Surgical Recovery and Length of Hospital Stay

Recovery from an operation will depend on the scale of the procedure undertaken and the preoperative state of the patient. An elective straightforward minimally invasive procedure over five thoracic vertebral levels with no preoperative deficit will typically involve a hospital stay of between 3 and 5 days in this patient group. A cervical vertebrectomy with anterior stabilization alone will be closer to 2 days.

11 Interventional Radiological Procedures

11.1 Vertebroplasty

Vertebroplasty is the fluoroscopically guided, percutaneous injection of bone cement into a vertebral body. Vertebroplasty will not relieve spinal cord compression; however, it can be helpful in relieving mechanical pain and stabilizing a vertebra at risk of fracture, particularly if the disease is within the vertebral body. As vertebroplasty is minimally invasive, it does not require a prolonged healing time before other treatments can be started.

11.2 Tumor Embolization

Very vascular tumors, such as renal carcinoma, may be rendered easier to treat surgically if embolized by a neuroradiologist and thereby made less vascular, prior to operation. Embolization can be performed using particles, coils, glue, or ethylene vinyl alcohol and may also contribute to reduction in a pain and neurological symptoms.

11.3 Image-Guided Tumor Ablation

There are a variety of radiological ablative techniques available, such as radiofrequency ablation, microwave ablation, thermal ablation, and cryoablation. These are typically used to treat painful metastases or as further treatment to areas previously irradiated. They are not used to treat acute spinal cord compression.

12 Radiotherapy

Radiotherapy is the mainstay of treatment for spinal cord compression and is given in combination with surgery, when appropriate. The main aims of radiotherapy are to reduce tumor bulk and pressure on the spinal cord and/or nerve roots, consolidate the mechanical benefit from surgery, and hopefully provide durable tumor control. Therefore, in a similar way to surgery, the overall goals with radiotherapy are to:

1. Prevent further neurological deterioration.
2. Restore neurological function.
3. Reduce pain.

It is important to note that even in the situation where any neurological improvement is unlikely,

radiotherapy can still potentially palliate symptoms of pain and improve quality of life. The maximal benefits from radiotherapy usually takes 4–6 weeks to occur, so this needs to be considered in making decisions.

There are two main types of radiotherapy: conventional external beam radiotherapy and stereotactic radiotherapy, which will be discussed in more detail below. Radiotherapy can be given as a single dose or fractionated into several smaller doses. Prior to starting radiotherapy, all patients should be considered for a full spine MRI, and commenced on corticosteroids (up to 16 mg dexamethasone a day in divided doses) as soon as the diagnosis is suspected. There is little evidence that higher doses are more effective (George et al. 2015; Loblaw and Mitera 2012), but serious adverse events are frequently higher with high-dose steroids, as expected. If the patient is receiving concurrent cytotoxic chemotherapy or immunotherapy, the potential increased risk of side effects with the radiotherapy needs to be considered and discussed with the patient and medical oncologist. Early radiotherapy-associated toxicities (e.g., esophagitis or erythematous skin reaction) tend to peak approximately 7–10 days after radiotherapy is completed and are specific to the area treated. They should be monitored and managed until resolution occurs. Late radiation reactions are rare in this setting.

12.1 Radiotherapy Simulation (Set-Up Position and Planning)

For radiotherapy to be effective, it needs to deliver the prescribed dose to the correct location within the body, with an accuracy of millimeters. This is achieved by ensuring the patient has adequate analgesia prior to simulation and each treatment and is able to lie in a comfortable and reproducible position. Often a patient-specific molded vacuum bag is used to help keep the patient immobilized in a comfortable position, together with small tattoo marks that are used to line the patient up in the correct position via laser beams on the treatment machine (Fig. 11a, b). A CT simulation image is usually acquired prior to starting treatment, and the radiotherapy is planned from this. In an emergency this process is simplified and often condensed to a single step.

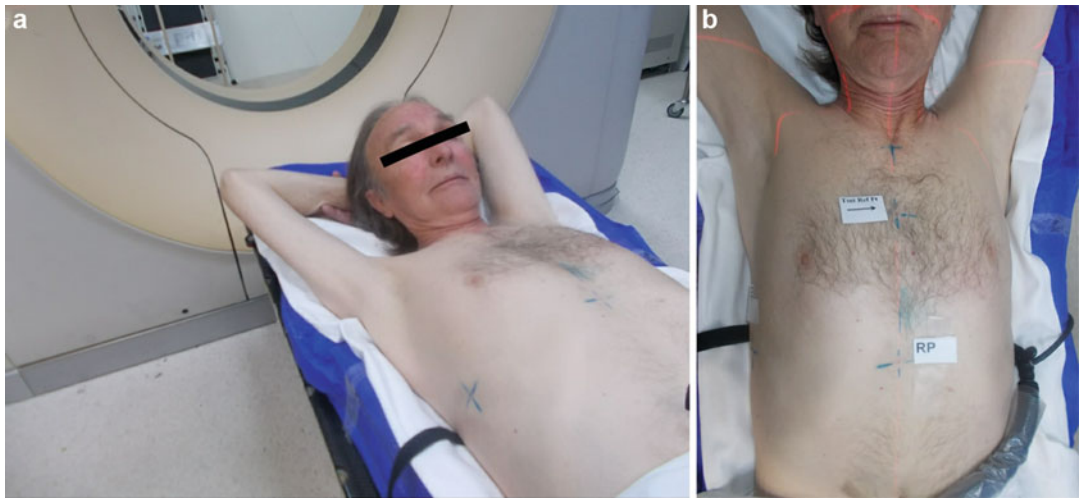

Fig. 11 (**a**) Patient lying supine on radiotherapy CT simulation couch for planning purposes. Blue vacuum bag is under patient. (**b**) Close-up photograph of treatment reference points (to be tattooed). This will assist with repositioning patient in the same position for radiotherapy treatment

12.2 Types of Radiotherapy

Conventional external beam radiotherapy is the most common technique used to treat spinal cord compression. It is a noninvasive method of delivering radiation to the tumor and surrounding structures (often the vertebral body above and below the level of concern) and is usually delivered using one to three radiotherapy beams (Fig. 12), depending on the location of the spinal cord or cauda equina compression. The radiation beams are shaped as they come out of the linear accelerator before they reach the patient to ensure they are directed at the tumor.

Stereotactic radiotherapy is another noninvasive technique but is more conformal using many smaller beams entering the body from a number of different angles. This means the radiotherapy dose distribution more closely matches the tumor and vertebral body (Fig. 13), avoiding nearby structures (particular organs at risk) compared with conventional external beam

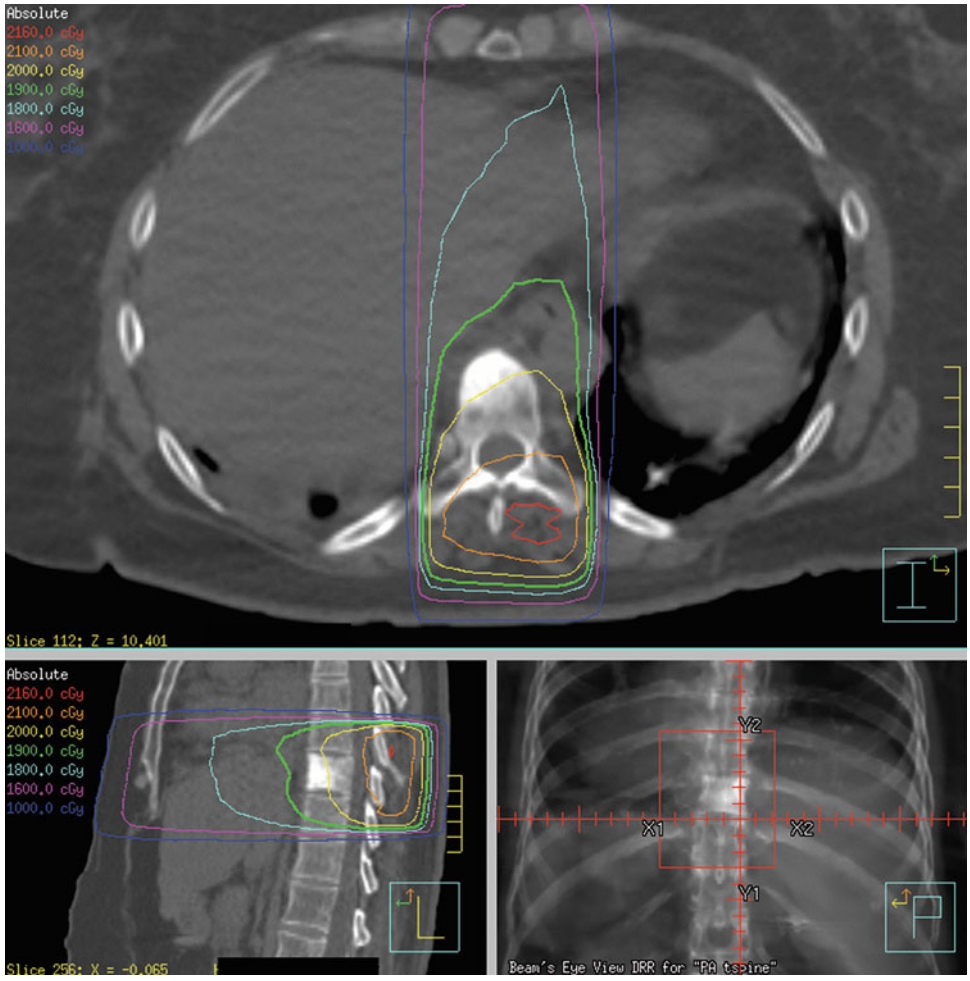

Fig. 12 Dosimetry of a conventional external beam radiotherapy plan for a patient with a single bone metastasis at T9 level. A single posterior beam is delivered, to a total dose of 20 Gy in five daily fractions. The green line is 95% of the prescribed dose. There is exit dose through the liver and stomach, potentially causing some mild temporary nausea

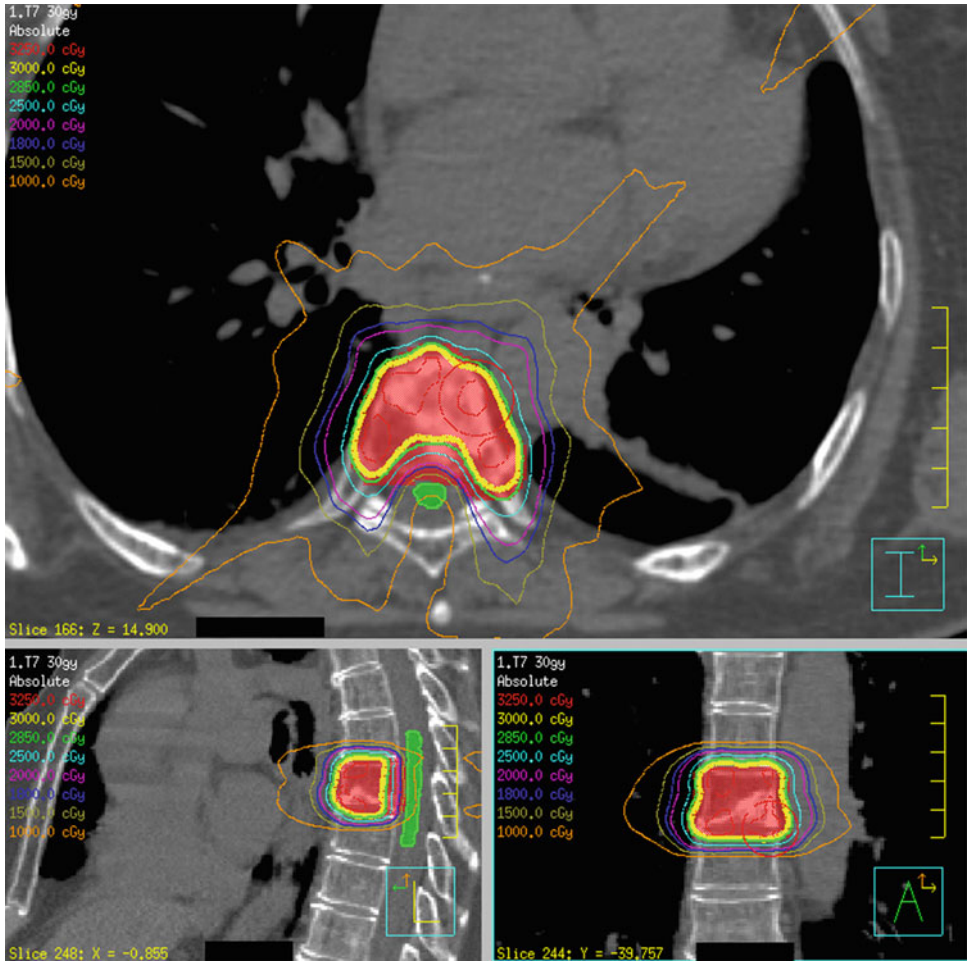

Fig. 13 Dosimetry of a stereotactic radiotherapy plan for a patient with a single bone metastasis at T7 level. Nine beams are delivered, to create a total dose of 30 Gy in four daily fractions. The yellow line is 100% of the prescribed dose and can be seen wrapping around (and therefore sparing) the spinal cord. There is minimal exit dose as the dose is highly conformal, therefore less toxicity to nearby organs

radiotherapy (Faculty of Radiation Oncology, The Royal Australian and New Zealand College of Radiologists 2017). Stereotactic radiotherapy is able to deliver a higher biological dose because it is better able to avoid normal healthy tissues and therefore requires tighter margins, a stricter set-up, and the patient to be very compliant and immobile during treatment planning and delivery. This higher biological dose may be particularly beneficial for tumor histologies (e.g., sarcoma, renal cell carcinoma, and melanoma) that have traditionally been regarded as relatively radioresistant.

While conventional external beam radiotherapy is widely available and easily delivered, stereotactic radiotherapy is more complex and may not be available in all situations. Stereotactic radiotherapy is unlikely to be used in an emergency situation because of the additional time required for planning and treatment verification. There are however two main advantages with stereotactic radiotherapy. Firstly, in a non-emergency situation for a patient with good prognosis disease, who has limited spinal metastases, the radiation oncologist may want to increase the radiotherapy dose to hopefully improve local

control in the longer term (Loblaw and Mitera 2012). This may be given preoperatively (prior to insertion of surgical hardware) so that the radiotherapy dosimetry and treatment verification are more accurate. The second benefit of stereotactic radiotherapy is for patients who have had previous external beam radiotherapy to the same spinal level and have a good performance status and a malignancy with a good prognosis. In this situation there may be an opportunity to offer re-treatment with stereotactic radiotherapy, with the advantage of sparing the spinal cord (avoid dose being deposited there) and a reduction in the treatment volume (therefore avoiding other normal tissues receiving additional dose). These are complex decisions and treatments requiring multidisciplinary discussion. Currently in the United States, the RTOG 0631 trial is comparing stereotactic radiotherapy with conventional external beam radiotherapy and includes patients with a limited (one to three) number of spine metastases, with or without minimal extradural compression (RTOG Foundation Inc 2016).

12.3 Dose Fractionation

The radiation oncologist chooses the "best-fit" radiotherapy dose and fractionation schedule, depending on the factors that were listed earlier in Fig. 8. The total dose and the number of radiotherapy treatment fractions (#s) vary widely (George et al. 2015). Various doses are acceptable for conventional external beam radiotherapy, including a single 8 Gy #, 16 Gy in 2 × 8 Gy#s delivered 1 week apart, 20 Gy in five daily #s delivered over a week, or 30 Gy in 8#s delivered over 2 weeks (4 days break in the middle of split course). Consideration should also be given to weekend treatment, especially early on in a fractionated course, or with the single doses. Higher doses may be considered for patients who are of excellent performance status, have limited disease, and have a long disease natural history. Stereotactic spine radiotherapy dose schedules also vary widely and include single 8–24 Gy fractions and multi-fraction dose schedules of 27–30 Gy in 3–5#s (Huo et al. 2017).

12.4 Efficacy and Outcomes

Radiotherapy is the most widely used treatment in the management of malignant spinal cord compression. A Cochrane Review (George et al. 2015) included six randomized trials ($n = 544$) of which Patchell et al. (2005) was the only trial to compare surgery with radiotherapy (RT) versus radiotherapy alone. This trial reported the following outcomes:

- Overall ability to walk after treatment was 84% (surgery + RT, RR 0.67, CI 0.53–0.86) vs. 57% (RT alone) (Patchell et al. 2005).
- Ability to walk was maintained by 94% (surgery + RT) vs. 74% (RT alone) ($p = 0.024$), with the median length of time able to walk being 153 days (surgery + RT) vs. 54 days (RT alone) ($p = 0.024$).
- Regaining ability to walk after treatment was achieved by 62% (surgery + RT) vs. 19% (RT alone) ($p = 0.01$), with non-ambulant surgical patients walking for a median of 59 days vs. 0 days (RT alone) ($p = 0.04$)
- Median survival was 126 days (surgery + RT) vs. 100 days (RT alone) ($p = 0.033$).
- Serious adverse effects (perforated gastric ulcer, psychosis, and death due to infection) were reported in 17% of patients receiving high-dose corticosteroid (96–100 mg dexamethasone) vs. 0% in moderate-to-low-dose (10–16 mg dexamethasone) patients (George et al. 2015).

This Patchell study excluded patients with poor prognosis (<3 months survival), multiple levels of spinal cord compression, and radiosensitive tumors (lymphomas, leukemia, multiple myeloma, and germ-cell tumors). It is important to note that patients with pathological fractures and spinal instability were included in the randomization, a situation which radiotherapy alone would not be expected to reverse and may have contributed to the poorer ambulatory outcomes in the radiotherapy-alone arm. A requirement of the trial was neurosurgical anterior decompression within 24 h of diagnosis, which may not be achievable in many settings. Again it is important

to note that even in patients with poor-prognosis disease, not suitable for surgery, or where neurological deficit reversal is unlikely, radiotherapy alone may still improve pain control and hence overall quality of life.

In terms of radiotherapy dose fractionation, the evidence suggests that single-fraction radiotherapy 8 Gy is just as effective as multiple fractions in patients with poor prognosis (<6 months survival) and no indication for primary surgery (diagnostic doubt, vertebral instability, bony impingement as the cause of spinal cord compression, or previous radiotherapy of the same area). No significant differences in overall survival, ambulation, duration of ambulation, pain response, and bladder control were reported in the two randomized controlled trials (Maranzano and Bellaviat 2005; Maranzano and Trippa 2009) comparing dose schedules (single versus multiple fractions) in these poor-prognosis patients.

For patients with a good prognosis, the use of surgery and radiotherapy should be considered where appropriate. Local tumor recurrence (within the radiotherapy field) may be more common, and consequently re-treatment rates higher, with a single dose, compared with higher-dose short-course radiotherapy schedules. Hence in patients who are expected to live longer, higher doses of radiotherapy are often prescribed, despite minimal evidence comparing radiotherapy schedules in patients with spinal cord compression and a good prognosis (George et al. 2015).

12.5 Early and Late Toxicities

Early radiotherapy toxicities are usually temporary, occurring midway during the radiotherapy course, peaking within 7–10 days of finishing, and usually resolving within approximately 4 weeks of radiotherapy course completion. These side effects will vary depending on the level of the spinal cord compression being treated (other organs/tissues within the RT field) and the dose delivered and may include:

- Esophagitis
- Nausea and vomiting (if the stomach in the radiotherapy field)
- Diarrhea (if bowel in the radiotherapy field)
- Alopecia (within the radiotherapy field only)
- Pneumonitis (if a significant volume of the lung is within the radiotherapy field)
- Skin reaction (includes itch, erythema, dry desquamation, but rarely moist desquamation at these lower doses) where the radiotherapy enters or exits the body
- Fatigue which is *independent* of the radiotherapy site and instead related presumably to cytokine release

Late radiotherapy toxicities are rare at these low palliative doses but may be permanent, usually occurring months to years after radiotherapy. Chronic progressive myelopathy is the main late side effect that must be considered. The estimated risk of myelopathy is low (<1%) for the conventional external beam radiotherapy dose schedules described above but may increase with dose-escalated stereotactic radiotherapy schedules (if spinal cord dose is not appropriately avoided) or in re-treatment settings (Kirkpatrick et al. 2010).

12.6 Re-treatment for Recurrent Spinal Cord Compression

Patients should be followed up clinically and/or radiographically to determine whether a local relapse develops. As with the first spinal cord compression diagnosis, prognosis, the probability of neurological recovery, and time to neurological recovery are highly dependent on pretreatment neurological status (Loblaw and Perry 2005). Patients should be considered for surgical decompression with or without radiotherapy first, because salvage rates seem to be better despite higher complication rates (Patchell et al. 2005). If a patient is not medically and surgically operable, radiotherapy with or without steroids should be given. Consideration needs to be given to the cumulative dosage of the combined radiotherapy courses, and therefore technique of radiotherapy

should be chosen to keep the cumulative dose of radiotherapy as low as possible to reduce the risk of myelopathy. Newer radiotherapy techniques such as stereotactic radiotherapy can be used to minimize cord dose (Loblaw and Mitera 2012; Ryu et al. 2010).

13 Systemic Treatments

A detailed explanation of all systemic agents that may be beneficial in patients with malignant spinal cord compression is beyond the scope of this chapter. Systemic agents include cytotoxic chemotherapy, immunotherapy, biological targets, hormonal therapy, and bisphosphonates. Each of these may have a role in different tumor subtypes, depending on the background performance status of the patient, burden of disease, previous systemic therapies received, and likelihood of benefit versus expected toxicities. However, these systemic agents are usually not suitable as primary treatment in the emergency setting for acute malignant spinal cord compression. Instead radiotherapy, surgery, or a combination of both is required.

For certain tumor biologies, the inclusion of systemic agents is of greater importance. In the case of multiple myeloma, although surgery and radiotherapy remain the primary approaches to treat malignant spinal cord compression, systemic therapy such as chemotherapy agents with steroids and either proteasome inhibitors or immunomodulatory drugs, with or without high-dose chemotherapy and stem cell transplantation, works rapidly and can be used instead of radiation in selected patients if there is minimal neurological deficit (Sen and Yavas 2016).

14 Supportive Care

Supportive care of all patients presenting with spinal cord compression is of utmost importance. This includes commencing corticosteroids, appropriate analgesia and aperients, exclusion/management of hypercalcemia, consideration of insertion of an indwelling urinary catheter, attention to pressure care, thromboprophylaxis, and referral to allied health and palliative care services if not already in place. The option of "best supportive care" without the active intervention of surgery and/or radiotherapy should always be considered and discussed with the patient and family if appropriate. Anxiety and depression are common in patients with cancer, and a referral to a psychosocial practitioner should be considered (eviQ Cancer Treatments Online (Cancer Institute NSW) 2012).

15 Conclusion

Spinal cord compression needs to be considered in all patients who have a malignancy and present with new or escalating back pain and/or abnormal neurology. Spinal cord compression is an emergency that must be diagnosed quickly, ideally with an MRI of the whole spine, urgent multidisciplinary input, and management instigated promptly. The best outcomes occur when the degree of premorbid neurological deficit is minimal and the diagnosis and treatment initiated within 24–48 h of presentation. Decompressive surgery with stabilization, followed by radiotherapy, in appropriately selected patients should be considered for best outcomes. Short courses or single fractions of radiotherapy (without surgery) are appropriate for patients with a predicted survival of less than 3 months, particularly if they are ambulant and have radiosensitive disease. Radiotherapy given to patients with very poor prognosis may still improve pain levels and quality of life, despite minimal improvement in neurological function.

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