The spinal column is the most frequent site of bone metastases, with 5 to 10% of cancer patients developing spinal metastases during the course of their disease. There is multiple non-contiguous involvement in up to 38% of patients. As would be expected there is a significant risk of spinal cord compression, ranging from 22% of breast cancer patients, 15% of lung carcinoma patients and 10% of prostatic carcinoma patients developing compression.

This common condition has significant morbidity during the patient’s remaining life. As life expectancy increases with oncological intervention, we are forced to make difficult decisions as to if and when spinal surgery should be employed.

Presentation
As with many spinal disorders, spinal metastases present with the triad of pain, neurological deficit and instability. Pain is the most common symptom. This pain is due to two main causes. The first is tumour-related. The pain is typically nocturnal or early morning and improves with activity. It is thought to be due to the release of inflammatory mediators and stretching of the periosteum of the involved expanding vertebral body. This pain tends to respond to steroids and local radiotherapy.

Mechanical pain, however, is due to a structural abnormality where the tumour has caused destruction. It is typically activity-related, and is aggravated by sitting or standing. Generally, the patient requires narcotics to control the pain and often bracing or surgical stabilisation.

Neurological deficit often starts in a radicular pattern of pain and progresses to a myelopathy if the compression is above the conus. There is frequently loss of sphincter control, which is important to detect and manage early as once lost for more than 24 hours, is unlikely to return. It is important to avoid neurological compromise as pre-intervention neurological status determines outcome.

Instability goes hand in hand with the aforementioned neurological status and pain, as it may be the cause of both. As illustrated in the case example (Figure 1) with collapse of T5, there was paraparesis as evidenced by the MRI cord signal, yet not severe stenosis. Intra-operatively it was evident that the lymphomatous destruction of the vertebral body had caused instability with both excessive translation and flexion/extension movements demonstrable. Once the body height and stability had been restored the patient had resolution of pain and rapid neurological recovery.

The spinal surgeon might be faced with a pathological fracture as the presenting complaint. There may not be a known underlying diagnosis and one is often forced to deal with the instability without a diagnosis, due to time pressure. Figure 2 is a case example of a young man presenting with a lumbar pain for a few weeks, followed by acute, severe pain. He had an anterior procedure to debulk, biopsy and stabilise. The cause turned out to be a melanoma. The primary was never found but the patient is alive at three years.
Patients often present with atypical back pain. The doctor needs to be alert and not to let these cases slip past as just another degenerative back pain. Red flags (Table I) such as night pain, onset of symptoms in old age or a history of previous tumour should raise the index of suspicion.

Investigation

Patients often present with atypical back pain. The doctor needs to be alert and not to let these cases slip past as just another degenerative back pain. Red flags (Table I) such as night pain, onset of symptoms in old age or a history of previous tumour should raise the index of suspicion.

Table I: Red flags that should raise suspicion that pain is atypical

- Presentation under age 20 years or onset over the age of 55 years
- Violent trauma, e.g. fall from a height, car accident
- Constant, progressive, non-mechanical pain
- Thoracic pain
- History of previous cancer
- Systemic steroids
- Systemically unwell
- Weight loss
- Persisting severe restriction of lumbar flexion
- Widespread neurological signs and symptoms
- Structural deformity
After a thorough history and clinical examination looking for the primary, the mainstay of orthopaedic investigation is the X-ray. Unfortunately X-rays are insensitive and require around 50% of bony destruction before there is radiological change. Even then it may be subtle (Figure 3).

Use of the bone scan will identify osteoblastic response in the spine and the rest of the skeleton. This will assist with identifying other bony sites. However, it has a low yield for osteolytic tumours such as myeloma.

The magnetic resonance imaging (MRI) scan is the best spine investigation and should be considered mandatory to assess a spinal metastasis should active management be indicated. This modality will assist with identifying non-contiguous lesions, detecting soft tissue extension and assessing cord compression. Tumour displaces bone marrow fat, and is hypointense compared to normal marrow on the T1 sequence. Tumour is hyperintense on T2 sequences, but with newer, faster spin echo T2 sequences, this change may be lost. Fat suppression techniques such as STIR are extremely useful and may be the most sensitive to identify tumour. They do however give less anatomical detail. Unfortunately it is difficult to differentiate tumour from osteomyelitis and osteoporotic fractures on MRI, which can often be a diagnostic dilemma. They are best differentiated on the T1 sequence. Osteoporotic fractures are more commonly thoracic, lack signal change or have band-like abnormalities, and do not involve the pedicle or have contour abnormality. Pathologic fractures showed homogeneously decreased signal and convex vertebral contour. The fractures involved the pedicles and were lumbar in location.

Newer PET scans are being utilised but currently indications for use are not clear.

Blood investigations would include routine full blood count and electrolytes. Often there are metabolic derangements due to other organ involvement or co-morbidities due to their health status. The ESR is useful to differentiate tumour from a benign cause of pain, but can be normal in some cases of tumour. An altered clotting profile is indicative of hepatic dysfunction and suggests liver tumour involvement.

Calcium is important as frequently these patients are hypercalcaemic, which can cause confusion and requires medical control. White cell markers are available to assist in identifying a gastrointestinal primary. Protein electrophoresis will identify myeloma.

A prostatic specific antigen (PSA) level should be requested in men. Urine analysis may reveal haematuria, which may be indicative of renal or bladder carcinoma.

Although the underlying tumour is often known, there is up to a 20% incidence of a second different histological type of tumour. Not infrequently one is presented with the case of an unknown primary and a tissue biopsy is necessary. Computerised tomography (CT) or fluoroscopically controlled biopsies by the surgeon under general anaesthesia are utilised.

Investigation is best done within a multi-disciplinary environment, and an oncologist’s input should be sought.

**Management options**

Metastatic spine disease is a common condition with a poor general prognosis, yet causes significant morbidity. There are multiple management options available, but should they be employed?

The least aggressive option is supportive care. This can be employed when the situation is futile and death is imminent.
Medical agents
Tumour symptoms and progression may be controlled by the use of chemotherapy. The use of chemotherapy consists of specific anti-tumour agents which are of limited value in metastatic disease. Steroids are useful. Dexamethasone (16-96 mg daily) reduces vasogenic oedema, reduces pain and may stabilise neurological deficits. Care should be taken in the unknown tumour, due to oncolytic effects of steroids. In tumours such as lymphoma, steroids induce cell death thus precluding histological diagnosis. Therefore they should be withheld until histological confirmation is obtained. Bisphosphonates are particularly useful in lytic tumours such as breast carcinoma. They have been shown to reduce the incidence of pathological fractures and surgical intervention in stage IV breast cancer.14

Radiotherapy (RT) has been the mainstay in controlling spinal metastases. Success depends on a differential susceptibility to ionising radiation between the tumour and normal cells. Radiosensitivity depends on the cells’ rate of proliferation, the stage of the cell cycle and degree of cell oxygenation. A double strand DNA break is considered lethal, and lesser damage is considered sublethal with the probability of cell survival being a function of absorbed dose.

Early RT side effects involve the rapidly proliferating tissues such as skin, bone marrow and mucosal surfaces, whereas the late effects are on the slower proliferating tissues, such as spinal cord and nerves. The acute reactions are not usually severe and late onset myelopathy can occur months to years later. Normal tissue tolerance limits the total RT dose, in this case usually the spinal cord. The difference in cell RT susceptibility and natural reparative process in sublethal damage is exploited to eradicate the tumour and limit normal cell death. This is done by fractionation, where the total dose is divided into a series of doses, allowing the less susceptible cells to repair themselves in-between doses. The commonly used regimen is 30 Gray in 10 divided doses. Due to the particular reparative time of spinal cord tissue, daily doses are utilised. The calculated risk of spinal cord injury with this regimen is 1%, but it appears lower in clinical practice. Fractionation, however, does increase the total dose required to achieve a biologically effective dose as even the more susceptible tumour cells will undergo some degree of repair.15

Before the routine utilisation of MRI and CT, radiotherapy was done to two vertebral bodies above and below and the target level. This was done due to uncertainty as to the exact position of the tumour and the experience of recurrence at contiguous sites, probably missed on X-ray/bone scan investigation. With CT and MRI one can be more precise about both position and contiguous involvement.

Conventional external beam RT has been effective in pain control in around 90% of cases, but there are limitations due to concerns regarding side effects. There have been recent advances in improving effectiveness without increasing side effects. Advances include intra-operative radiotherapy16 where the spinal cord can be shielded and radiation applied directly to the tumour. Due to logistic difficulties this is not widely used.

With modern imaging, treatment planning and delivery systems a highly conformal dose of radiation can be delivered accurately to almost any region of the body. Three-dimensional conformal RT and intensity modulation RT are examples.17 The latter technique allows a volume of radiotherapy to be administered to an anatomical region in a non-homogeneous fashion, thus varying the dose to each specific area. This mapping allows sparing of the vulnerable structures such as the spinal cord, but of course requires accurate positioning which is technically difficult. The extreme case is radiosurgery or Cyberknife technology, where a single high dose is applied to a focal target with accuracies of 1.5 mm with the use of robotic control.18,19

Surgery
In addition, surgery is an option. Surgery is palliative in metastatic disease, although there are proponents for cure in the solitary metastasis scenario. There is an extreme range of surgery available. This extends from stabilisation for pain control, debulking the tumour mass to prevent or delay neurological compromise and optimise oncological agents to the more aggressive en bloc resections.

The spine may be approached from posterior, such as in posterior pedicle screw/rod stabilisation,20,21 or ventrally for anterior decompression and fusion,22,23 which is commonly employed when there is cord compression. The approaches may be combined when rigid stabilisation from posterior is required in anterior decompression.24 Newer techniques offer anterior and posterior column surgery, all from the posterior approach.19 The latter technique is used for en bloc resection of the metastasis.25,26,27 This may be indicated in the case of a solitary metastasis22 or a radio-insensitive tumour.

Vertebroplasty is increasingly used for pain control in metastatic disease where there is body infiltration with loss of body height up to 30%. This technique offers a relatively non-invasive method of surgical stabilisation.25

Surgery has been shown to control pain in the vast majority of cases, but brings complications of infection of around 5% and hardware failure of 3%.26 It of course adds significant cost to the management of these patients.

There may be a role for pre-operative embolisation in renal cell and thyroid tumours due to their vascularity. However a minimal difference in blood loss has been reported by King,2 although the incidence of abandoning surgery is higher in the non-embolised group.

With all these options it is necessary to review the literature to make some sense of it all. Ryken et al.28 provided an evidence-based review of the surgical management of spinal metastatic disease. In their literature review, they found only one class I study.
This older study from 1980 compared laminectomy plus RT, with RT alone. They had limited outcome measures, but found no difference between the two groups. This put a damper on surgical intervention for many years.

However, subsequent to this, Patchell et al.\(^2\) published on 101 cases of spinal metastases with spinal cord compression. In this randomised control study, the surgery and RT group maintained ambulation longer than RT alone – this being 122 days versus 13. There was a higher chance of regaining function with surgery and they concluded that direct decompression with RT was better than RT alone.

There are multiple class 2 and 3 studies in the literature.\(^1\) Sundaresan\(^2\) showed improved ambulation rates with surgery. Others refuted this but claim improvement in pain control with surgery. Some showed improvement in bladder function. However, there seems consensus that surgery does not affect survival rates.

In terms of timing of RT, Ghogawala\(^2\) showed increased sepsis rates with pre-operative RT. This was confirmed by Sundaresan.\(^2\) It is recommended that post-operative RT be delayed until wound healing around six weeks after surgery.

Ryken et al.\(^1\) concluded that there was insufficient evidence to recommend a treatment standard, but felt that surgery is beneficial as it alleviates pain and improves patients’ quality of life.

From the literature it is apparent that despite increasing surgical complexity and cost, there is no clear change in survival. There may be longer maintenance of ambulation, but this is possibly due to earlier intervention in recent studies versus older studies. But are these the correct outcome measures to look at? A recent meeting of the Global Spine Tumour Group stresses that quality of life, pain and hospital stay are also important.\(^2\)

There are patients who fare better than the rest and it is necessary to select those for treatment. Hosono et al.\(^3\) identified tumour type, pre-operative pain and paresis as predictors of outcome.

Tomita et al.\(^3\) were the first to provide a scoring system to evaluate patients with a view to outcome. They suggested scoring the tumour type, including the presence of visceral and bony metastases. With a low score, the goal should be long-term local control and aggressive surgery was indicated. A high score correlated with short life expectancy and supportive care was indicated.

Tokuhashi et al.\(^3\) also developed a scoring system, which was revised in 2005 (Table II). This revision showed an improved correlation of prediction and survival of 86%. The evaluation system looked at the general condition of the patient, the number of extraspinal and spinal metastases, the primary tumour and the neurological status. Again a total score was used to decide on conservative care, palliative surgery and excisional surgery. The higher the score, the longer the expected survival of the patient.

### Table II: Revised Tokuhashi scoring system for evaluation of prognosis

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Score</th>
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<tbody>
<tr>
<td>General condition (performance status)</td>
<td></td>
</tr>
<tr>
<td>Poor (KPS 10%–40%)</td>
<td>0</td>
</tr>
<tr>
<td>Moderate (KPS 50%–70%)</td>
<td>1</td>
</tr>
<tr>
<td>Good (KPS 80%–100%)</td>
<td>2</td>
</tr>
<tr>
<td>No. of extraspinal bone metastases foci</td>
<td></td>
</tr>
<tr>
<td>≥3</td>
<td>0</td>
</tr>
<tr>
<td>1–2</td>
<td>1</td>
</tr>
<tr>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>No. of metastases in the vertebral body</td>
<td></td>
</tr>
<tr>
<td>≥3</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Metastases to the major internal organs</td>
<td></td>
</tr>
<tr>
<td>Irremovable</td>
<td>0</td>
</tr>
<tr>
<td>Removable</td>
<td>1</td>
</tr>
<tr>
<td>No metastases</td>
<td>2</td>
</tr>
<tr>
<td>Primary site of the cancer</td>
<td></td>
</tr>
<tr>
<td>Lung, osteosarcoma, stomach, bladder,</td>
<td>0</td>
</tr>
<tr>
<td>oesophagus, pancreas</td>
<td></td>
</tr>
<tr>
<td>Liver, gallbladder, unidentified</td>
<td>1</td>
</tr>
<tr>
<td>Others</td>
<td>2</td>
</tr>
<tr>
<td>Kidney, uterus</td>
<td>3</td>
</tr>
<tr>
<td>Rectum</td>
<td>4</td>
</tr>
<tr>
<td>Thyroid, breast, prostate, carcinoid tumour</td>
<td>5</td>
</tr>
<tr>
<td>Palsy</td>
<td></td>
</tr>
<tr>
<td>Complete (Frankel A, B)</td>
<td>0</td>
</tr>
<tr>
<td>Incomplete (Frankel C, D)</td>
<td>1</td>
</tr>
<tr>
<td>None (Frankel E)</td>
<td>2</td>
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</tbody>
</table>

Criteria of predicted prognosis (total score):

<table>
<thead>
<tr>
<th>0–8 &lt; 6 months</th>
<th>9–11 ≥ 6 months</th>
<th>12–15 ≥ 1 year</th>
</tr>
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</table>

These scoring systems assist in deciding which patients have a life expectancy that justifies surgical intervention. Once this is established, the magnitude of the procedure needs to be decided upon.

The goals of surgery are as follows:

- palliative
- focusing on reducing pain
- preserving neurological function
- maintaining/restoring function
### Conclusion

Despite the benefits for some patients, the role of surgery in metastatic spine disease is still to be defined. Care has to be taken to identify those patients who have a better life expectancy, and to limit the surgical insult in those less likely to live long. Individually planned management plans should be tailored to suit the patient with regard to predicted outcome, cost to the patient and cost to society. Here cost goes beyond financial cost and includes hospital stay and the additional morbidity of surgery. The decisions are even more challenging in a resource-limited environment such as exists in South Africa, but those patients with a better prognosis should be identified and actively managed to maximise the quality of their remaining life.

### References