MANAGEMENT OF METASTATIC TUMORS TO THE SPINE
5–10% of all cancer patients

70% of all patients develop metastatic disease

40% of all patients develop metastatic *spinal* disease

10–20% of these patients will develop epidural spinal cord compression (~20,000–30,000 cases/year)

**Location:**
Thoracic – 70%
Lumbar – 20%
Cervical – 10%
Introduction

Spine is the most common site of bony metastases

Median survival with spinal metastasis (SM)- 3 to 18 months

The highest incidence of SM is found in the 40–65 age-group as this is the period of highest cancer incidence
Vertebral and/or epidural (extradural) involvement is seen in 90–95% of SM.

Intradural extra-medullary and intra-medullary seeding of systemic cancer is unusual.

Lepto-meningeal disease occurs in about 10% of patients.
Introduction

Primary tumors most likely to metastasize to the vertebral column

a. breast (16–37%)
b. prostate (9–15%)
c. lung (12–15%)
d. kidney (3–6%)
e. thyroid (4%).

Metastases from prostate, breast, melanoma, and lung commonly cause spinal metastases in 90.5%, 74.3%, 54.5%, and 44.9% of patients
Introduction

Risk for neurological deficits due to epidural spinal cord compression varies with the site of primary disease:

- 22% with breast cancer
- 15% with lung cancer
- 10% with prostate cancer

Metastatic spinal disease arises in any of three locations:

- vertebral column (85%)
- paravertebral region (10% to 15%)
- rarely the epidural or subarachnoid and intramedullary space (<5%)
**Introduction**

The posterior half of the vertebral body is involved first, with the anterior body, lamina, and pedicles usually affected later.

Multiple lesions at non-contiguous levels occur in 10% - 40%.

10% patients have an unknown primary (in 50% lung will be the primary source).

Most metastatic lesions are osteolytic. Only 5% of metastases have an osteoblastic response.
Pathways of spread

✓ arterial route

✓ venous routes through the Batson plexus

✓ direct invasion through the inter-vertebral

✓ lymphatics
Presentation

Night pain or pain when recumbent is a classic feature of spine malignancy (85–96%)

Pain almost always precedes the loss of neurological function

Pain: Tumor related- nocturnal
  Mechanical- vertebral destruction

Motor dysfunction is the second most common (35–75%)
Diagnosis

- Baseline neurologic exam- Grade the patient

- X-ray- limited role as 30-50% of vertebral body needs to be destroyed before involvement can be seen

- Bone scans- highly sensitive, identifies areas of increased bone deposition. So, easily detects osteoblastic metastases but can only detect osteolytic lesions if there is a significant bone repair occurring
Diagnosis

- CT scan- sensitivity and specificity of CT to detect bony involvement ranges between 90% and 100%

- MRI whole spine (about 15% patients will have other lesions) has the greatest sensitivity (98.5%) and specificity (98.9%) with overall accuracy of 98.7%
Diagnosis

- CT myelography – when MRI can’t be done or when an MRI is not available. Can cause neurological worsening if done in presence of high-grade block rostral to the puncture.

- PET/SPECT

- Angiography

- Biopsy
Grading Scales
### Frankel Grading Scale

<table>
<thead>
<tr>
<th>GRADE</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>No motor or sensory function</td>
</tr>
<tr>
<td>B</td>
<td>Preserved sensation only, no motor function</td>
</tr>
</tbody>
</table>
| C     | Nonambulatory, wheelchair bound, some motor function  
  a. Bowel or bladder paralysis  
  b. Neurogenic bowel or bladder  
  c. Voluntary normal bowel or bladder function |
| D     | Ambulatory but with neurological symptoms  
  1. Requires walker  
  2. Requires a cane  
  3. Can walk independently  
  a. Bowel or bladder paralysis  
  b. Neurogenic bowel or bladder  
  c. Voluntary normal bowel or bladder function |
| E     | Normal neurological functions |

## Eastern Cooperative Oncology Group (ECOG) Performance Status Grades

<table>
<thead>
<tr>
<th>GRADE</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Fully active, able to carry on all predisease performance without restriction</td>
</tr>
<tr>
<td>1</td>
<td>Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature (light housework, office work)</td>
</tr>
<tr>
<td>2</td>
<td>Ambulatory and capable of all self-care but unable to carry out any work activities; up and about &gt;50% of waking hours</td>
</tr>
<tr>
<td>3</td>
<td>Capable of only limited self-care, confined to bed or chair &gt;50% of waking hours</td>
</tr>
<tr>
<td>4</td>
<td>Completely disabled; cannot carry on any self-care; totally confined to bed or chair</td>
</tr>
<tr>
<td>5</td>
<td>Dead</td>
</tr>
<tr>
<td>GRADE</td>
<td>DESCRIPTION</td>
</tr>
<tr>
<td>------------------</td>
<td>----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>A (complete)</td>
<td>No motor or sensory function is preserved through S4-5</td>
</tr>
<tr>
<td>B (incomplete)</td>
<td>Sensory but no motor function is preserved below the neurological level and extends through S4-5.</td>
</tr>
<tr>
<td>C (incomplete)</td>
<td>Motor function is preserved below the neurological level, and most key muscles below the neurological level have a muscle grade &lt;3</td>
</tr>
<tr>
<td>D (incomplete)</td>
<td>Motor function is preserved below the neurological level, and most key muscles below the neurological level have a muscle grade ( \geq 3 ).</td>
</tr>
<tr>
<td>E (normal)</td>
<td>Motor and sensory function are normal.</td>
</tr>
</tbody>
</table>
# Gait Scale

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Normal</td>
</tr>
<tr>
<td>2</td>
<td>Gait with assistance</td>
</tr>
<tr>
<td>3</td>
<td>Paresis without gait function but still able to move legs</td>
</tr>
<tr>
<td>4</td>
<td>Paraplegia</td>
</tr>
</tbody>
</table>
Management Principles

Options: Surgery, Radiation, Chemotherapy

Early intervention: as neurological outcome after treatment is primarily dependent on the neurological status before treatment.

Primary histology and post-treatment ambulatory status - most consistently determine survival (median survival for breast CA- 650 days, lung cancer -120 days).

Decision issues- ambulatory function, pain control, autonomic function (sexual and bowel/bladder control), overall survival, and quality of life.

Surgery should only be offered to patients with an estimated life expectancy of greater than 3 to 6 months.
Staging

**Harrington’s scheme** (based on bone destruction & neurological compromise)

1. no significant neurological involvement
2. involvement of bone without collapse or instability
3. major neurological impairment (sensory or motor) without significant involvement of bone
4. vertebral collapse with pain resulting from mechanical causes or instability, but with no significant neurological compromise
5. vertebral collapse or instability combined with major neurological impairment

**Recommendation:** Cat 1, 2 & 3 - CT, RT or hormonal Tx
Cat 4 & 5 – Surgery

Staging

Based on definition of spinal instability:

1. Kostuik et al: Two-column concept

- Anterior column - vertebral body, further into ant./post & left/right

- Posterior column - pedicles, laminae & spinous processes; further into left/right

- Spine unstable if ≥ 3 segments were destroyed

Staging

2. Tomita et al: Instability present if there was-

- transitional deformity
- vertebral body collapse greater than 50%
- three column involvement (as defined by Denis)
- involvement of the same column in two or more adjacent levels

Staging

3. **Cybulski** –
   
a) Anterior and middle column destruction (> 50% collapse of VB ht.)
   
b) Collapse of 2 or more adjacent VBs
   
c) Tumor involvement of the middle and posterior columns
   
d) Previous laminectomy, with failure to recognize anterior and middle column disease

**Recommended**- Sx decompression and fixation when any one of above criteria, presence of neural compression in patients with life expectancy > 5–6 months, competent immune and nutritional status, incomplete neurological deficit, and a radioresistant tumor or a tumor that failed to respond to previous treatment

**SINS Score**

- Range 0-18
- 0 - 6 denotes stability
- 7- 12 denote indeterminate (possibly impending) instability
- 13- 18 denote instability
- Patients with SINS scores of 7 to 18 warrant surgery


Prognostic Scoring Systems
**Tomita Scoring System**

1 point - Slow growth: Breast, Thyroid, Prostatic, Testicular CA

2 points - Moderate growth: Renal cell, Uterus, Ovarian, Colorectal CA

4 points = Rapid growth: Lung, Gastric, Esophageal, Nasopharyngeal, Hepatocellular, Pancreas, Bladder, Melanoma, Sarcoma (osteosarcoma, Ewing sarcoma, Leiomyosarcoma), Other rare ca., Primary unknown metastasis

Rare CA (4 points): Inflammatory type Breast CA, undifferentiated Thyroid CA, inflammatory type Renal cell CA
Treatments: Medications

**Steroids**

Used in metastatic disease causing spinal cord dysfunction

Rationale- reduces vasogenic edema, protects against lipid peroxidation & hydrolysis, enhances blood flow, prevents ischemia and intracellular calcium accumulation, stabilizes lysosomal membranes, attenuates inflammatory response, and supports cellular energy metabolism

Dosage- Loading doses 10 -100 mg, followed by 4 to 24mg QDS
Treatments: Medications

Sorensen et al. compared high-dose dexamethasone f/b RT with RT alone- 81% patients in the steroid group were ambulatory after treatment compared with 63% in the control group.

Heimdal et al. showed that in patients with a complete myelographic block who received a bolus of 100 mg followed by a standard maintenance dose had no better pain relief, ambulation, or bladder function than those who received a 10-mg bolus and the same maintenance therapy.

Recommendation- initial bolus of 10 mg followed by 16 mg/day


Treatments: Medications

**Bisphosphonates**
Work by inhibiting osteoclast activity and thus decreasing bone resorption. Also have direct tumoricidal effect.

Many RCTs evaluated the use of bisphosphonates in the prevention of skeletal-related events (SREs), defined as pathologic #, spinal cord compression, RT or Surgery for bone metastases, or hypercalcemia. Bisphosphonates showed to decrease the number of and time to an SRE in prostate cancer, breast cancer, multiple myeloma, lung cancer, and renal cell carcinoma.
Treatments: Medications

Hormone Therapy

Most commonly for breast and prostate cancer

Breast cancer- Selective estrogen receptor modulators (SERM) such as tamoxifen, and aromatase inhibitors such as letrozole, anastrozole, and exemestane have been shown to be effective

Prostate cancer- androgen suppression with GnRH agonists and/or flutimide are effective

Even if the primary tumor is responsive to hormone therapy, metastases may not possess the same hormone receptors, therefore, may be unresponsive to hormone therapy
Surgery

Indications for surgery

- Radioresistant tumors (sarcoma, lung, colon, renal cell, breast)
- Obvious spinal instability
- Clinically significant neural compression secondary to retropulsed bone or from spinal deformity
- Intractable pain unresponsive to nonoperative measures
- Radiation failure (progression of deficit during treatment or spinal cord tolerance reached)
Surgery

Historically, laminectomy was the only surgical treatment offered.

Complications (11%)- wound infection/dehiscence and spinal instability

Decompressive laminectomy was prone to failure because in most cases the tumor is ventral to the thecal

Laminectomy can cause/ worsen preexisting spinal instability leading to progressive deformity & pain & neurological compromise

Recommendation- done when pathology is strictly confined to the lamina and spinous process
## Ambulatory Outcome after Various Treatments

<table>
<thead>
<tr>
<th>Treatment</th>
<th>N</th>
<th>Success (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Posterior Decompressive Laminectomy Alone</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Mean success- 30%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Barron, 1959</td>
<td>38</td>
<td>29</td>
</tr>
<tr>
<td>Wild, 1963</td>
<td>22</td>
<td>26</td>
</tr>
<tr>
<td>Brice and Mckissock, ‘65</td>
<td>139</td>
<td>32</td>
</tr>
<tr>
<td>Stark, 1982</td>
<td>32</td>
<td>16</td>
</tr>
<tr>
<td>Findlay, 1987</td>
<td>80</td>
<td>24</td>
</tr>
<tr>
<td>Sorensen, 1989</td>
<td>105</td>
<td>34</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Treatment</th>
<th>N</th>
<th>Success (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Radiation Alone</em> (Mean success- 47%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mones et al, 1966</td>
<td>41</td>
<td>34</td>
</tr>
<tr>
<td>Khan et al, 1967</td>
<td>82</td>
<td>41</td>
</tr>
<tr>
<td>Gilbert et al, 1978</td>
<td>170</td>
<td>49</td>
</tr>
<tr>
<td>Constans et al, 1983</td>
<td>108</td>
<td>39</td>
</tr>
<tr>
<td>Sorensen et al, 1989</td>
<td>149</td>
<td>38</td>
</tr>
<tr>
<td>Ruff &amp; Lanska, 1989</td>
<td>41</td>
<td>73</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Treatment</th>
<th>N</th>
<th>Success (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>PDL and Radiation</em> (Mean- 47%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mullan and Evans, 1957</td>
<td>21</td>
<td>43</td>
</tr>
<tr>
<td>Wild and Porter, 1963</td>
<td>23</td>
<td>44</td>
</tr>
<tr>
<td>Wright, 1963</td>
<td>17</td>
<td>47</td>
</tr>
<tr>
<td>Constans et al, 1983</td>
<td>465</td>
<td>46</td>
</tr>
<tr>
<td>Sherman, 1986</td>
<td>111</td>
<td>57</td>
</tr>
<tr>
<td>Sorensen et al, 1989</td>
<td>91</td>
<td>53</td>
</tr>
</tbody>
</table>

*Success is defined as the ability to walk after the operation (i.e., gait was maintained, improved, or regained as a result of the laminectomy)*
Surgery

Laminectomy alone or in combination with radiation was no more effective in terms of preserving or restoring neurological function than radiation alone.

In a review of 134 patients treated with either a laminectomy ($n = 111$) or laminectomy with stabilization ($n = 23$), Sherman and Waddell found that the latter group had better posttreatment ambulatory status (92% versus 57%), sphincter function, and pain control and less recurrent neurological dysfunction.

Surgery

**Anterior decompression**

One of the first reported series performing anterior spinal decompression was in 1982 by Siegal and coworkers.

Approaches can broadly be classified as anterior (e.g., transthoracic, retroperitoneal) or posterior, including posterolateral trajectories (e.g., laminectomy, transpedicular, costotransversectomy, lateral extracavitary)
Surgery

Consensus and data are lacking as to the optimal surgical approaches and procedures and are at the discretion of the treating surgeon.

Patients with metastatic spinal disease requiring surgical intervention may be treated with either an en bloc spondylectomy (considered in the rare patient with a solitary metastasis and favourable prognosis) or more commonly with an intrallesional decompression and stabilization.
Surgical Classification Schemes
Percutaneous vertebral augmentation

1. Vertebroplasty - injection of (PMMA) cement into vertebral body

2. Kyphoplasty

3. Skyphoplasty
Radiation

Indications-

- Radiosensitive tumors (lymphoma, multiple myeloma, small cell lung carcinoma, seminoma of testes, neuroblastoma, Ewing's sarcoma)
- Survival <3- 4 months
- Inability to tolerate an operation, total
- Neurological deficit for more than 24 -48 hours
- Multilevel or diffuse spinal involvement
Radiation

Standard radiation portal involves the diseased level with a 5-cm margin, which effectively includes two vertebral bodies above and below.

Long course RT: 30-40 Gy in 20-30 #
Short course RT: 16 Gy in 1-2 # or 20 Gy in 5 # (very sick pts.)

Average pain improvement, ambulatory success, and rescue in recent RT trials are 77%, 63%, and 29%
# First Score (predicts survival after RT)

<table>
<thead>
<tr>
<th>First Score</th>
<th>(%)Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>6 mtnths</td>
</tr>
<tr>
<td>20-25</td>
<td>4</td>
</tr>
<tr>
<td>26-30</td>
<td>11</td>
</tr>
<tr>
<td>31-35</td>
<td>48</td>
</tr>
<tr>
<td>36-40</td>
<td>87</td>
</tr>
<tr>
<td>41-45</td>
<td>99</td>
</tr>
</tbody>
</table>

Radiation

Recommendation-

Score 20-30: short-course therapy

Score > 36 points: long-course therapy

Score 31 to 35 points: gray zone
Van der Linden's Scoring System

<table>
<thead>
<tr>
<th>Prognostic factors</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>KPS</strong></td>
<td></td>
</tr>
<tr>
<td>80-100</td>
<td>2</td>
</tr>
<tr>
<td>50-70</td>
<td>1</td>
</tr>
<tr>
<td>20-40</td>
<td>0</td>
</tr>
<tr>
<td><strong>Primary tumor</strong></td>
<td></td>
</tr>
<tr>
<td>Breast</td>
<td>3</td>
</tr>
<tr>
<td>Prostate</td>
<td>2</td>
</tr>
<tr>
<td>Lung</td>
<td>1</td>
</tr>
<tr>
<td>Other</td>
<td>0</td>
</tr>
<tr>
<td><strong>Visceral mets</strong></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1</td>
</tr>
<tr>
<td>Yes</td>
<td>0</td>
</tr>
</tbody>
</table>

- 0 to 3 points - 3 months OS
- 4 to 5 points - 9 months OS
- 6 points - 18.7 months OS
Stereotactic Radiosurgery

Indications: No consensus

✓ Limited (i.e. 1–3 metastases)

✓ ≤ 2 contiguous vertebral bodies involved

✓ Limited and/or controlled systemic disease

✓ Good performance status

✓ Anticipated survival > 3 months
Stereotactic RT

- Long-term pain control - 86%,
- Tumor control - 90%,
- 84% of patients with neurological deficits experienced some clinical improvement
Intramedullary Spinal Cord Metastases

Rare < 5% patients

Most common source - lung carcinoma (esp. SCLC)

When to suspect? -- patient with h/o malignancy and new onset of unilateral motor or sensory impairments

Brown-Sequard syndrome: 30–45%
Intramedullary Spinal Cord Metastases

Hallmark - rapid progression of neurological symptoms (primary intramedullary tumors - slow growing and present with a gradual progression of symptoms)

75% patients progressed to full neurological deficit within 1 month of the initial development of neurological symptoms

Intramedullary metastases are generally a late finding
Intramedullary Spinal Cord Metastases

Average survival is less than 1 month

General recommendation-

Sensitive tumors- XRT

Resistant tumors- microsurgical resection (often discrete, well circumscribed tumors) combined with treatment of the primary tumor and other secondary metastases
Patient with suggestive history

- Confirm with biopsy

- Grade the patient- Frankel/ ECOG/ ASIA

- Calculate survival- Tokuhashi/ Tomita/ SINS score

- Decide mode of treatment that may be offered- Conservative/ palliative/ excisional

- Decide the route of surgery
Thank You