Management of Painful Metastatic Tumors of the Spine

UCSF Spine Symposium 2013

Michael W. Groff, MD
Director of Spinal Neurosurgery

Brigham and Woman’s Hospital
Harvard Medical School

Disclosures

Depuy Spine
Consulting
Grant support

Biomet Spine
Consulting
Grant support

Goals: NOMS

Neurologic
• Decompression

Oncologic
• Resection

Mechanical Stability
• Instrumented Fusion

Systemic Disease
• Death or Prolonged Hospital Stay

Mark Bilsky

Oncologic: Tumor Pathology

Metastatic
• Palliation
• Intra-lesional
• Adjuvant therapy

Primary
• Cure
• En bloc
• Limited adjuvant
Incidence of Spinal Metastases

40-60% of cancer patients harbor spinal metastasis
- 10% are symptomatic
18,000 new cases annually in NA
Most common malignant spine tumor
Most common site of bone metastasis

Metastatic Cord Compression

Histology is unknown at presentation in 10% of cases with metastatic spinal cord compression
50% of those cases will turn out to have lung cancer

Primary Tumor

<table>
<thead>
<tr>
<th>Tumor</th>
<th>Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>22%</td>
</tr>
<tr>
<td>Lung</td>
<td>15%</td>
</tr>
<tr>
<td>Myeloma</td>
<td>9%</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>7%</td>
</tr>
<tr>
<td>GI</td>
<td>5%</td>
</tr>
<tr>
<td>Prostate</td>
<td>10%</td>
</tr>
<tr>
<td>Renal</td>
<td>6%</td>
</tr>
<tr>
<td>Thyroid</td>
<td>3%</td>
</tr>
</tbody>
</table>

Spinal Level

<table>
<thead>
<tr>
<th>Spinal Level</th>
<th>Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thoracic</td>
<td>70%</td>
</tr>
<tr>
<td>Lumbar</td>
<td>20%</td>
</tr>
<tr>
<td>Cervical</td>
<td>10%</td>
</tr>
</tbody>
</table>

Probability of met = f (number of bodies, size of bodies)
**Location Within Body**

Vertebral body  85%
- Early involvement of pedicle
Paravertebral  15%
Epidural space  5%
Intradural  rare

**Manifestations of Spine Metastases**

Back Pain
Cord Compression
Pathologic fracture - 8% incidence
- 53% are breast cancer

---

**“Metastatic” Back Pain**

Most common presentation
Constant dull ache
Progresses to frank pain
Awakens from sleep
Aggravated by valsala

Etiology
- Tumor spread/tissue destruction
- Periosteal innervation
- Cord compression
- Spinal instability
- Nerve root irritation

Pain onset to neuro signs
avg 7 mos

[Hatrick et al, Radiother Onc 2000]

---

**Pathologic Fracture**

50% destruction required
[Edelstyn et al, Clin Radiol 1967]
**Pathologic Fracture**

**Results of Treatment for Spinal Cord Compression: Radiotherapy Alone**

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Patients (n)</th>
<th>% Improved</th>
<th>% Worse</th>
<th>% Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mones et al.</td>
<td>1966</td>
<td>41</td>
<td>34</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Khan et al.</td>
<td>1967</td>
<td>82</td>
<td>42</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Cobb et al.</td>
<td>1977</td>
<td>18</td>
<td>50</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>Gilbert et al.</td>
<td>1977</td>
<td>29</td>
<td>41</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>Marshall &amp; Langfitt</td>
<td>1977</td>
<td>130</td>
<td>49</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Greenberg et al.</td>
<td>1980</td>
<td>83</td>
<td>57</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Stark et al.</td>
<td>1982</td>
<td>31</td>
<td>35</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Constans et al.</td>
<td>1983</td>
<td>108</td>
<td>39</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>Obbens et al.</td>
<td>1984</td>
<td>83</td>
<td>28</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>Harrison et al.</td>
<td>1985</td>
<td>33</td>
<td>27</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>Bach et al.</td>
<td>1990</td>
<td>149</td>
<td>35</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>Maranzano</td>
<td>1995</td>
<td>209</td>
<td>76</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td><strong>Mean</strong></td>
<td></td>
<td>-</td>
<td>44</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td>996</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Results of Treatment for Spinal Cord Compression: Laminectomy with or without Radiotherapy**

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Patients (n)</th>
<th>% Improved</th>
<th>% Worse</th>
<th>% Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hall &amp; McKay</td>
<td>1973</td>
<td>129</td>
<td>30</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Brady et al.</td>
<td>1975</td>
<td>90</td>
<td>61</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Merrin et al.</td>
<td>1976</td>
<td>22</td>
<td>22</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Cobb et al.</td>
<td>1977</td>
<td>26</td>
<td>46</td>
<td>23</td>
<td>-</td>
</tr>
<tr>
<td>Gilbert et al.</td>
<td>1977</td>
<td>65</td>
<td>45</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Marshall &amp; Langfitt</td>
<td>1977</td>
<td>17</td>
<td>29</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Gianotta &amp; Kindt</td>
<td>1978</td>
<td>33</td>
<td>30</td>
<td>18</td>
<td>12</td>
</tr>
<tr>
<td>Kleinman et al.</td>
<td>1978</td>
<td>20</td>
<td>15</td>
<td>5</td>
<td>15</td>
</tr>
<tr>
<td>Livingston &amp; Perrin</td>
<td>1978</td>
<td>100</td>
<td>58</td>
<td>-</td>
<td>0</td>
</tr>
<tr>
<td>Baldini et al.</td>
<td>1979</td>
<td>140</td>
<td>30</td>
<td>19</td>
<td>0</td>
</tr>
<tr>
<td>Gorter</td>
<td>1979</td>
<td>31</td>
<td>39</td>
<td>-</td>
<td>13</td>
</tr>
<tr>
<td>Dunn et al.</td>
<td>1980</td>
<td>104</td>
<td>33</td>
<td>23</td>
<td>10</td>
</tr>
<tr>
<td>Levy et al.</td>
<td>1982</td>
<td>39</td>
<td>82</td>
<td>15</td>
<td>8</td>
</tr>
<tr>
<td>Stark et al.</td>
<td>1982</td>
<td>84</td>
<td>37</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Constans et al.</td>
<td>1983</td>
<td>465</td>
<td>46</td>
<td>13</td>
<td>-</td>
</tr>
<tr>
<td>Klein et al.</td>
<td>1984</td>
<td>194</td>
<td>54</td>
<td>16</td>
<td>-</td>
</tr>
<tr>
<td>Kolliann et al.</td>
<td>1984</td>
<td>103</td>
<td>56</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Garcia-Picazo et al.</td>
<td>1990</td>
<td>53</td>
<td>41</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Back et al.</td>
<td>1990</td>
<td>91</td>
<td>59</td>
<td>11</td>
<td>-</td>
</tr>
<tr>
<td>Landmann et al.</td>
<td>1992</td>
<td>127</td>
<td>58</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td><strong>Mean</strong></td>
<td></td>
<td>1953</td>
<td>44</td>
<td>13</td>
<td>7</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td>996</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Results of Treatment for Spinal Cord Compression: Laminectomy (Posterior Decompression) and Stabilization**

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Patients (n)</th>
<th>% Motor Improved</th>
<th>% Pain Improved</th>
<th>% Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brunon et al.</td>
<td>1975</td>
<td>20</td>
<td>-</td>
<td>100</td>
<td>-</td>
</tr>
<tr>
<td>Hansebout et al.</td>
<td>1980</td>
<td>82</td>
<td>84</td>
<td>100</td>
<td>-</td>
</tr>
<tr>
<td>Miles et al.</td>
<td>1984</td>
<td>23</td>
<td>65</td>
<td>100</td>
<td>-</td>
</tr>
<tr>
<td>DeWeald et al.</td>
<td>1985</td>
<td>17</td>
<td>45</td>
<td>65</td>
<td>6</td>
</tr>
<tr>
<td>Overby et al.</td>
<td>1985</td>
<td>12</td>
<td>75</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Solini et al.</td>
<td>1985</td>
<td>33</td>
<td>48</td>
<td>-</td>
<td>3</td>
</tr>
<tr>
<td>Heller et al.</td>
<td>1986</td>
<td>33</td>
<td>70</td>
<td>79</td>
<td>-</td>
</tr>
<tr>
<td>Perrin et al.</td>
<td>1987</td>
<td>200</td>
<td>82</td>
<td>80</td>
<td>8</td>
</tr>
<tr>
<td>Olerud</td>
<td>1996</td>
<td>51</td>
<td>38</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>Bauer</td>
<td>1997</td>
<td>67</td>
<td>76</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>Bilsky</td>
<td>1999</td>
<td>25</td>
<td>90</td>
<td>-</td>
<td>12</td>
</tr>
<tr>
<td><strong>Mean</strong></td>
<td></td>
<td>67</td>
<td>89</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td>563</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Results of Treatment for Spinal Cord Compression: Vertebral Body Resection and Stabilization

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Patients (n)</th>
<th>Improved Motor %</th>
<th>Improved Pain %</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slatkin and Posner</td>
<td>1982</td>
<td>29</td>
<td>56</td>
<td>60</td>
<td>7</td>
</tr>
<tr>
<td>Harrington</td>
<td>1984</td>
<td>52</td>
<td>65</td>
<td>80</td>
<td>6</td>
</tr>
<tr>
<td>Siegal and Siegal</td>
<td>1985</td>
<td>51</td>
<td>80</td>
<td>91</td>
<td>6</td>
</tr>
<tr>
<td>Sundaresan et al.</td>
<td>1985</td>
<td>101</td>
<td>70</td>
<td>85</td>
<td>8</td>
</tr>
<tr>
<td>Onimus et al.</td>
<td>1986</td>
<td>36</td>
<td>72</td>
<td>97</td>
<td>6</td>
</tr>
<tr>
<td>Perrin &amp; McBroom</td>
<td>1987</td>
<td>21</td>
<td>95</td>
<td>90</td>
<td>5</td>
</tr>
<tr>
<td>Moore &amp; Uttley</td>
<td>1989</td>
<td>26</td>
<td>62</td>
<td>71</td>
<td>30</td>
</tr>
<tr>
<td>Sundaresan et al.</td>
<td>1991</td>
<td>54</td>
<td>100</td>
<td>90</td>
<td>6</td>
</tr>
<tr>
<td>Hall &amp; Webb</td>
<td>1991</td>
<td>15</td>
<td>86</td>
<td>-</td>
<td>20</td>
</tr>
<tr>
<td>Fidler</td>
<td>1994</td>
<td>18</td>
<td>93</td>
<td>94</td>
<td>20</td>
</tr>
<tr>
<td>Hosono et al.</td>
<td>1995</td>
<td>90</td>
<td>81</td>
<td>94</td>
<td>0</td>
</tr>
<tr>
<td>Gokaslan et al.</td>
<td>1998</td>
<td>72</td>
<td>78</td>
<td>92</td>
<td>3</td>
</tr>
<tr>
<td><strong>Mean</strong></td>
<td></td>
<td><strong>76</strong></td>
<td><strong>85</strong></td>
<td><strong>10</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td><strong>575</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Management Goals

**Neurologic function**
- No effect on longevity

**Oncologic**
- Intractable pain
- Risk of collapse

**Mechanical stability**
- (Systemic disease)

### Work-up

**History**
- Ambulation, B/B, Pain worse at night

**Physical exam**
- LE weakness, long tract signs, sensory level, point tenderness

**MRI of the spine - compression**

**CT of the spine - stability**

**Restage primary**
- CT chest, abdomen, and pelvis
- FDG PET
- 10 - 30% with synchronous lesions

**Labs with LFT’s**

### Localization

<table>
<thead>
<tr>
<th>Root</th>
<th>C5</th>
<th>C6</th>
<th>C7</th>
<th>L4</th>
<th>L5</th>
<th>S1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motor</td>
<td>Deltoid</td>
<td>Biceps</td>
<td>Triceps</td>
<td>Quads</td>
<td>Dorsiflexion</td>
<td>EHL</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Plantarflexion</td>
<td></td>
</tr>
<tr>
<td>Sensory</td>
<td>Upper arm</td>
<td>Thumb &amp; index finger</td>
<td>3rd digit</td>
<td>Anterior thigh</td>
<td>Lat leg, dorsum of foot</td>
<td>Sole of foot</td>
</tr>
<tr>
<td>Reflex</td>
<td>Biceps</td>
<td>Supinator</td>
<td>Triceps</td>
<td>Patellar</td>
<td>None</td>
<td>Achilles</td>
</tr>
</tbody>
</table>
Stability Assessment

Anatomic
- 2 column
- 3 Column

Physiologic
- History positional pain

Trauma is not Oncology

Case EW

66 year old man
C2 metastasis of non-small cell lung CA
Severe neck pain
Neurologically intact
Metastasis to liver

What to do?

Do No Harm
Case CM

48 year old woman
LE weakness, back pain
Metastatic osteosarcoma from hip
What to do?

Post op - 1 year

MRI

Study of choice
Unsuspected lesions in 30%
Whole body fast-imaging techniques:
- STIR 30-45 min
- Echo-planar 6 min

False positives
Radionuclide Imaging

50-80% more sensitive than plain films
Detection up to 18 mos earlier

[Pagani & Libshitz, Radiol Clin North Am 1982]

2% cold

55 yo prostate CA & LBP

SPECT

SPECT more sensitive, better localization
Benign: ↑ uptake in endplate, lateral body border, facet, spinous process
Malignant: ↑ uptake in pedicle, central body, entire vertebra, cold lesions with ↑ uptake at margins

[Sedonja et al, Clin Nucl Med 1999]

MRI vs Bone Scan

Bone scan assesses cortical bone
Early lesions small and intramedullary
MRI more sensitive
Bone scans more cost effective

Taoka et al, AJR 2001
Myelography

Risk of LP below high-grade block
Use high cervical cisternal puncture
Be prepared for emergent OR

Importance of Biopsy

Metabolic bone disease
(osteoporosis & osteomalacia)
Benign tumors
Myeloma/plasmacytoma
Primary bone sarcomas
Paget’s disease
DDX - CT guided biopsy
  • Core bx preferable to FNA

Breast CA

50 year old woman
Back and leg pain
Worse s/p XRT
Known Breast CA
Only known met

Intraop - LECA
Renal Cell CA

<10% cases
Median survival 6-9 months historically
5-yr survival 10-50%
10-yr survival 5-30%
Improved adjuvant therapy
Standard radiation therapy not effective
Conformal radiation
Preop embolization very helpful
Renal Cell

59 year old woman
S/P T12 resection of renal cell met
Index resection shortly after nephrectomy
Local recurrence 3 years post op
Presents w/ paraparesis, kyphosis, HW failure

CT Myelogram

Postop

Immediately postop worse RLE weakness
Ambulating without assistance at 3 months
Importance of embolization
  • Prabhu et al JNS 2003
  • Jackson et al JNS 2001
**Study Design**

All patients
- Underwent MRI
- Treated with Decadron
- Diagnosis confirmed with biopsy

Stratification based on
- Tumor type
- Ambulatory status
- Spine stability

Randomized to
- surgery with XRT or XRT alone (30Gy)

**Entry Criteria**

- Known cancer
- Symptomatic lesion
- Resectable based on MRI
- Not paraplegic > 48 hours
- No prior XRT

Exclusion: lymphoma, leukemia, multiple myeloma, germ cell tumor, primary spinal tumor

---

**Treatment**

Radiation started within 24 hours
Surgery within 24 hours

Goals
- Remove as much tumor as possible
- Immediate decompression
- Stabilization when needed

XRT started less than 14 days post-op

---

**Direct decompressive surgical resection in the treatment of spinal cord compression caused by metastatic cancer: a randomised trial**

**Summary**
Background: The standard treatment for spinal cord compression caused by metastatic cancer is corticosteroids and radiotherapy. The role of surgery has not been established. We assessed the efficacy of direct decompressive surgery.

Methods: In this randomised, multi-institutional, non-blinded trial, we randomly assigned patients with spinal cord compression caused by metastatic cancer to either surgery followed by radiotherapy (n = 51) or radiotherapy alone (n = 51). Radiotherapy for both treatment groups was given in ten 3 Gy fractions. The primary endpoint was the ability to walk. Secondary endpoints were Karnofsky score, muscle strength and functional status, the need for corticosteroids and opioid analgesics, and survival time. All analyses were by intention to treat.

Findings: After an interim analysis of the study was stopped because of a predetermined early stopping rule, there was 123 patients were assessed for eligibility before the study closed (101) were randomised. Significantly more patients in the surgery group (67.2%) than in the radiotherapy group (23.7%) were able to walk after treatment (odds ratio 2.10 [95% CI 1.49-2.94] p = 0.001). Patients treated with surgery also retained the ability to walk significantly longer than did those with radiotherapy alone (n = 12 days vs 11 days, p = 0.001). 32 patients entered the study unable to walk; significantly more patients in the surgery group regained the ability to walk than patients in the radiotherapy group (28/32 [92%] vs 13/31 [42%], p = 0.001). The need for corticosteroids and opioid analgesics was significantly reduced in the surgical group.

Interpretation: Direct decompressive surgery plus postoperative radiotherapy is superior to treatment with radiotherapy alone for patients with spinal cord compression caused by metastatic cancer.
Endpoints

Primary
• Ambulation
Secondary
• Continent
• ASIA and Frankel grade
• Narcotic and steroid use
• Survival

Results

Ambulation
• Surgery + XRT 126 days
• XRT alone 35 days
• For non-ambulatory patients 56% vs 19%

Continent
• Surgery + XRT 142 days
• XRT alone 12 days

Survival
• Surgery + XRT 129 days
• XRT alone 100 days

Steroid use 1.6 mgs vs 4.2 mgs
Narcotic use 0.4 mgs Morphene vs 4.8 mgs
Complications Post-op 12%
• Hardware/ fusion - half
• Wound breakdown – half

Conclusion

Surgery + XRT is superior to XRT alone for symptomatic Spinal Column Metastasis.
Vertebroplasty for Tumor

Originally applied to osteoporotic burst fractures
Addresses the structural deficiencies of the anterior column
An adjunct to either
• XRT
• Surgery

Complications

Anterior Column Augmentation
Predicting Spinal Collapse

Collapse = f(tumor size & location, loading, BMD)
- Tumor size exponential increase
- Finite element analysis
  - Whyne et al Spine 2003
  - Roth et al Clin Orthop 2004

Costovertebral joint or pedicle involvement increases risk of collapse
Loading is related to spinal level (C,T,L)

Spinal Radiosurgery

Evolution of intracranial radiosurgery
Minimally invasive
Steep radiation fall off curve
- Avoids radiation toxicity to spinal cord
- Allows higher tumorcidal doses to tumor

Radiosensitive Metastasis

<table>
<thead>
<tr>
<th>Tumor</th>
<th>Control</th>
<th>Shrinkage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>Good</td>
<td>Good</td>
</tr>
<tr>
<td>Lung (small cell)</td>
<td>Poor</td>
<td>Good</td>
</tr>
<tr>
<td>Renal</td>
<td>Worst</td>
<td>Worst</td>
</tr>
<tr>
<td>Melanoma</td>
<td>Worst</td>
<td>Worst</td>
</tr>
<tr>
<td>Prostate</td>
<td>Poor</td>
<td>Good</td>
</tr>
<tr>
<td>Follicular Thyroid</td>
<td>Good</td>
<td>Poor</td>
</tr>
</tbody>
</table>
CyberKnife

0.3 mm accuracy
< 1 mm clinical accuracy
Arbitrary beams
Over 100 nodes
Over 1200 beams
Approximately $3 \times 10^6$

Summary

Treatment must be individualized
Patient’s quality of life must be emphasized
Anterior column reconstruction
Surgery for symptomatic lesions is on stronger footing than it has been
Other modalities are evolving as well