Spinal Neoplasia

- The spine is the most common site of skeletal metastatic disease. (70%)
- 40% of bony metastases involve the vertebrae
- 1 in more than 100,000 patients are affected yearly.
- Each year, more than 20,000 cancer patients (10-20%) with advanced disease develop epidural spinal cord compression, a medical emergency.
Spinal Neoplasia

- Patients experience back pain or neurologic compromise from spinal cord or nerve root impingement.

- Treatment for spinal metastases may include:
  - pain meds
  - Corticosteroids
  - systemic chemotherapy
  - Surgery
  - radiotherapy
Role of Spinal Neoplasia

- **Surgical treatment**
  - Safer and more feasible because of recent advances in technique and spinal instrumentation

  - Indicated for cases of tumor progression associated with:
    - spinal instability
    - pain or neural compression with acute or progressive neurologic decline
Spinal Neoplasia

- Relative Contraindication to Surgical treatment
  - Poor overall medical condition
  - Limited life expectancy
  - Widespread spinal disease
Conventional Radiotherapy

- **U.S.**
  - Conventionally fractionated external-beam radiotherapy (EBRT)
    - delivered over 5–20 days to a total dose of 20–40 Gy (most commonly 30 Gy in 10 fractions)

- **Europe**
  - single-fraction treatments of 8 Gy are common.
  - Provide short-term regression of tumor-related symptoms but often suboptimal for long-term control of extensive disease.
Problems with Conventional Radiotherapy

- **EBRT**
  - utilizes a relatively broad, unfocused energy beam that radiates all structures in its field.
  - Provides obvious treatment limitation, especially in cases of relatively radioresistant tumors in which toxicity to organs at risk
Problems with Conventional Radiotherapy

- EBRT
  - Can affect the overlying skin and fascial layers impeding wound healing in surgical patients.
  - Broad radiation fields may also affect clinically significant amounts of bone marrow and delay chemotherapy in patients with poor reserves.
Problems with Conventional Radiotherapy

- Up to 25% of patients may experience tumor progression within 2 years of treatment with conventional radiotherapy.

- Retreatment of these patients who have received prior radiation therapy is limited by the low tolerance of the spinal cord to irradiation.
Problems with Conventional Radiotherapy

- Longevity and Slow Efficacy
  - Takes 4 weeks in some cases to complete a full treatment plan
  - Can take up to 3 months for success in palliative pain relief
Radiosurgery

- conceived by Lars Leksell of the Karolinska Institute in Sweden
- designed to deliver an ablative dose (1-5 fractions of >2-3 Gy) of targeted radiation to a lesion
- Has a rapid dose falloff, minimizing irradiation of surrounding normal structures.
Stereotactic radiosurgery (SRS)

- A well-established, accepted standard treatment for various intracranial targets.
- SRS for metastatic disease to the brain results in up to 85%–95% local tumor control.
- Intracranial frame-based fixation has been demonstrated to limit dose alignment error to 1 to 2 mm.
Stereotactic radiosurgery (SRS) in Spine

- Radiosurgical systems that use an invasive head frame for stereotactic immobilization are limited by the inability to treat the entire spine.

- The first report of spinal SRS in 1995 attempted to translate stereotactic principles to the treatment of spinal tumors. (Hamilton et. al. *Neurosurgery*, 1995)
Stereotactic radiosurgery (SRS)

- Fiducial frame was surgically attached directly to the spinous process, providing immobilization and accurate target localization.
- A linear accelerator (LINAC)-based system was used to irradiate the lesion, delineated on CT scanning.
- It demonstrated the feasibility and safety of using radiosurgery in the treatment of extracranial lesions.
Spinal radiosurgery

Smaller contour represents prescription dose line, large contour represents 50% of the prescription dose.

The isodose labeling refers to the percentage of prescription dose (800 cGy).

The intent was to keep the prescription dose line at least 5 mm from the spinal cord while keeping the spinal cord dose as low as possible.
Dosimetry-Hamilton et. al. 1995

- Dosimetry plan constructed so that the maximal dose delivered to any portion of the spinal cord was under 300 cGy
- The median number of isocenters was one (range, one to five) with a median single fraction dose of 10 Gy (range, 8-10 Gy)
- A median normalization of the 80% isodose contour was used (range, 80-160%).
# Results - Hamilton et. al. 1995

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Sex/Age</th>
<th>Tumor</th>
<th>Level</th>
<th>Thecal Sac Compression</th>
<th>Prior Radiation (Gy)/No. of Fractions</th>
<th>Radiosurgery Dose (Gy)</th>
<th>No. of Isocenters</th>
<th>% Normalization of Maximum Dose</th>
<th>Follow-up (mo)</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M/13</td>
<td>Osteosarcoma</td>
<td>L1</td>
<td>Yes</td>
<td>42/21</td>
<td>8</td>
<td>5</td>
<td>73</td>
<td>14</td>
<td>NVR; CLR</td>
</tr>
<tr>
<td>2</td>
<td>M/70</td>
<td>Metastatic adenocarcinoma</td>
<td>L2–L3</td>
<td>Yes</td>
<td>46/23</td>
<td>10</td>
<td>1</td>
<td>74</td>
<td>8</td>
<td>NVR; CLR</td>
</tr>
<tr>
<td>3</td>
<td>M/71</td>
<td>Metastatic renal cell</td>
<td>T5</td>
<td>No</td>
<td>33/11</td>
<td>10</td>
<td>1</td>
<td>69</td>
<td>1</td>
<td>Died ~1 mo(^b)</td>
</tr>
<tr>
<td>4</td>
<td>M/57</td>
<td>Adenocarcinoma lung</td>
<td>T3–T4</td>
<td>No</td>
<td>65/30</td>
<td>10</td>
<td>1</td>
<td>58</td>
<td>6</td>
<td>CLR (^c)</td>
</tr>
<tr>
<td>5</td>
<td>F/28</td>
<td>Metastatic breast</td>
<td>C7–T2</td>
<td>No</td>
<td>45/25</td>
<td>8</td>
<td>4</td>
<td>31</td>
<td>2</td>
<td>Died ~2 mo(^d)</td>
</tr>
</tbody>
</table>

\(^a\) NVR, no radiographically visible recurrence; CLR, clinical resolution of signs/symptoms.

\(^b\) Patient pain-free at treated site; died of metastatic liver disease.

\(^c\) 50% reduction in tumor volume.

\(^d\) Died at 2 months from intracranial hemorrhage; no clinical progression of disease at treated site.

Table 1. Stereotactic Spinal Radiosurgery Patient Summary\(^a\)
Results - Hamilton et al. 1995
Results - Hamilton et al. 1995
Although the clinical results seemed promising, the need for general anesthesia and the invasive spinal fixation required prevented wide application of this crude technique.

- It required placement of a surgical fiducial marker under general anesthesia
- Invasive and uncomfortable
- The prone positioning of the patient made the spine more susceptible to respiratory motion.
Intensity Modulated Radiosurgery
The Novalis Shaped-Beam system (BrainLAB)

6 mV linear accelerator (Coplanar radiation aimed at isocentric centers)

Varies dose of beam (5-9) in real times as it moves through various planes

Micro multileaf collimator uses 26 pairs of leaves to alter beam shape (inverse planning)

Radiation delivered through
- circular cone arcs
- fixed shape conformal beams
- fixed gantry using static or dynamic intensity modulation
Intensity Modulated Radiosurgery

Acquisition of CT with patient in body fixture and Exactrac which detects infrared fiducial markers (Precision: 0.3 mm)

Pretreatment CT compared to patient’s position

Images sent to planning station where CTV is outlined

Degree of variation: 1.36 mm; average deviation: 2%
Spinal radiosurgery (SRS) Novalis (BrainLab)

Only 10% of spinal cord receives 80% of prescribed dose
CyberKnife® (Accuray, Inc., Sunnyvale, CA)

- developed at Stanford University in 1994
- Non coplanar, non isocentric
- precisely aligns treatment beams with targets.
- Has three fundamental differences from conventional frame-based radiosurgery.
  - It references the position of the treatment site to internal radiographic features such as skeletal anatomy or implanted fiducials rather than frames
  - It uses real-time x-rays to establish the position of the lesion during treatment and dynamically brings the therapy beam into alignment with the observed position of the treatment site.
Third, it aims each beam independently, without a fixed isocenter.  
- Changes in patient position during treatment are compensated for by adaptive beam pointing 
- No need for reproduction of the position in the treatment planning study.
CyberKnife® (Accuray, Inc., Sunnyvale, CA)

Until recently fiducials (screws implanted in lamina) were necessary for this product
Accuracy: 0.7 mm (plus/minus 0.3 mm)
XSight
- 2D-3D local image registration performed which registers each pair of enhanced x-ray images to digitally reconstructed radiographs (DRR)
- DRR Possess high CT attenuation coefficients
CyberKnife® (Accuray, Inc., Sunnyvale, CA)

X Sight

- If a large movement of treatment site is detected, the position of the patient is corrected with an automatic movement of the couch
- Error: 0.49 mm
Inverse Planning

- Software attempts to find directions and doses for each beam to achieve desired dose distribution
- Beams not directed by hand

CyberKnife® (Accuray, Inc., Sunnyvale, CA)
Tomotherapy

- 6 Mv LINAC rotates as in a CT
- Irradiation delivered in oblique transverse planes through 64 binary multi-leaf collimators and given slice by slice
- Dose gradients of 10% per mm achieved
Spinal AVMs

T8-T9 Spinal AVM (juvenile)

Type III (juvenile) spinal cord AVM treated with 25 Gy delivered in five sessions of 5 Gy each. The thyroid gland is outlined as a critical structure.
Spinal AVMs

[Graph showing the number of fractions and the corresponding cGy doses over the years from 1997 to 2005.]

Spinal AVMs
Eradication of Glomus (Type 2) AVM

Pre SRS

Post SRS

Spinal AVMs
Eradication of Glomus (Type 2) AVM at C5-C6

Benign Lesions

Benign Lesions

51 patients

- 30 schwannomas
- 9 neurofibromas
- 16 meningiomas

Dose ranged from 16 to 30 Gy in 1-5 fractions

39% of lesions decreased in size (mean 36 months)

Pain relief in 50% of meningioma and 70% in schwannoma

One patient developed myelopathy (posterior column dysfunction)

Dodd, Robert L. M.D., Ph.D.; Ryu, Mi-Ryeong M.D., Ph.D.; Kamnerdsupaphon, Pimkhuan M.D.; Gibbs, Iris C. M.D.; Chang, Steven D. Jr M.D.; Adler, John R. Jr M.D.

CyberKnife Radiosurgery for Benign Intradural Extramedullary Spinal Tumors Neurosurgery: April 2006 - Volume 58 - Issue 4 - pp 674-685
Metastatic lesions

Antonio A. F. De Salles, M.D., Ph.D., Alessandra G. Pedroso, M.D., Paul Medin, Ph.D., Nzhde Agazaryan, Ph.D., Timothy Solberg, Ph.D., Cynthia Cabatan-Awang, R.N., N.P., Dulce M. Espinosa, M.D., Judith Ford, M.D., Ph.D., and Michael T. Selch, M.D.

Spinal lesions treated with Novalis shaped beam intensity-modulated radiosurgery and stereotactic radiotherapy  JNS (101), 2004
Metastatic lesions

**Table 1. Characteristics of the Treatment Group (n = 500)**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous external beam irradiation</td>
<td>344</td>
</tr>
<tr>
<td>Primary indications for radiosurgery treatment</td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td>336</td>
</tr>
<tr>
<td>Primary treatment modality</td>
<td>65</td>
</tr>
<tr>
<td>Tumor progression</td>
<td>51</td>
</tr>
<tr>
<td>Progressive neurologic deficit</td>
<td>32</td>
</tr>
<tr>
<td>Postsurgical treatment</td>
<td>9</td>
</tr>
<tr>
<td>Radiation boost</td>
<td>7</td>
</tr>
<tr>
<td>Levels treated</td>
<td></td>
</tr>
<tr>
<td>Cervical</td>
<td>73</td>
</tr>
<tr>
<td>Thoracic</td>
<td>212</td>
</tr>
<tr>
<td>Lumbar</td>
<td>112</td>
</tr>
<tr>
<td>Sacral</td>
<td>103</td>
</tr>
<tr>
<td>Skull tracking</td>
<td>68</td>
</tr>
<tr>
<td>Fiducial tracking</td>
<td>432</td>
</tr>
<tr>
<td>Mean/median tumor volume (range) 46/29 cm³ (0.20–264)</td>
<td>49/29 cm³ (0.20–264)</td>
</tr>
<tr>
<td>Mean maximum dose (range)</td>
<td>20 Gy (12.5–25)</td>
</tr>
<tr>
<td>Mean volume of spinal canal dose &gt;8 Gy</td>
<td>0.6 cm³</td>
</tr>
</tbody>
</table>

Fractionation schedules of prior irradiated patients:
- $3 \text{ Gy} \times 10$ to $2.5 \text{ Gy} \times 14$

### Table 2. Lesion Histopathologies (n = 500)

<table>
<thead>
<tr>
<th>Lesion Type</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal cell</td>
<td>93</td>
</tr>
<tr>
<td>Breast</td>
<td>83</td>
</tr>
<tr>
<td>Lung</td>
<td>80</td>
</tr>
<tr>
<td>Melanoma</td>
<td>38</td>
</tr>
<tr>
<td>Colon</td>
<td>32</td>
</tr>
<tr>
<td>Sarcoma</td>
<td>26</td>
</tr>
<tr>
<td>Prostate</td>
<td>24</td>
</tr>
<tr>
<td>Multiple myeloma</td>
<td>18</td>
</tr>
<tr>
<td>Unknown primary</td>
<td>14</td>
</tr>
<tr>
<td>Squamous cell (laryngeal)</td>
<td>12</td>
</tr>
<tr>
<td>Thyroid</td>
<td>11</td>
</tr>
<tr>
<td>Other</td>
<td>69</td>
</tr>
</tbody>
</table>
Metastatic lesions

Table 3. Summary of Pain and Radiographic Outcome for the 4 Most Common Histopathologies (n = 294)

<table>
<thead>
<tr>
<th>Long-term pain improvement</th>
<th>All patients</th>
<th>Renal cell</th>
<th>Breast</th>
<th>Lung</th>
<th>Melanoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>86%</td>
<td>94%</td>
<td>96%</td>
<td>93%</td>
<td>96%</td>
</tr>
<tr>
<td>Renal cell</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Melanoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Long-term radiographic control</th>
<th>All patients</th>
<th>Renal cell</th>
<th>Breast</th>
<th>Lung</th>
<th>Melanoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>88%</td>
<td>87%</td>
<td>100%</td>
<td>100%</td>
<td>75%</td>
</tr>
<tr>
<td>Renal cell</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Melanoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

-When used as a primary treatment modality, long-term tumor control was demonstrated on follow-up imaging in 90% of cases (in all breast, lung, and renal cell carcinoma metastases, and 75% of melanoma metastases).

-Seven cases with radioresistant tumors were treated with spinal radiosurgery with no tumor progression at the immediate adjacent levels.

42-year-old man with a painful melanoma metastasis of the T3 vertebral body. Prescribed dose of 18 Gy that was calculated to the 80% isodose line; the maximum tumor dose was 22.5 Gy. The tumor volume was 16.8 cm³ and the spinal cord received a maximum dose of 10 Gy.
Ideal Radiosurgical Dose

- 18-24 Gy ideal dose for most mets
- 8 or 10 Gy dose limitation to adjacent spinal cord volume
- Jin: limit 10% of the adjacent spinal cord volume to a dose less than 10 Gy
- Traditional tenet:
  - Spinal cord can tolerate 4500-6000 cGy in daily fractions of 180-200 cGy with a <5% risk of myelopathy in 5 yrs
Advantages

- Able to radiate usually radioresistant lesions such as melanoma, renal cell CA
Complications

- L’ Hermitte sign
- Acute paralysis secondary to ischemia
- Tissue necrosis
  - Limit to 8 Gy or less dose immediately adjacent to levels involved
- In-field failure
  - Need for follow up MRIs
Conclusions

- **Radiosurgery**
  - Still in infancy, however there is a clear role in the treatments of AVM, benign lesions, pain, and metastatic growth
  - Can be utilized as salvage treatment for those who have had external beam radiation
  - Ideal for
    - Limited spinal disease
    - Favorable overall performance status
    - Focal neurological symptoms