Objectives

- Briefly summarize key concepts for spine stereotactic radiosurgery (SRS)
- Discuss why spine SRS makes sense for benign tumors
- Review existing studies on spine SRS

SRS / SBRT as the Future of Radiation Oncology

- Minimize normal tissue radiation exposure which may help decrease late effects
- High dose per fraction has implications on the radiobiology of these tumors
  - Radioresistant histologies are more responsive to higher doses per fraction
  - Better control
- Shorter duration of treatment
  - Implications on costs which are in part driven by number of fractions

How to Deliver More Radiation?

- Stereotactic Radiosurgery
  - Concept partly developed by Lars Leksell
    - If one can use beams of radiation that converge at a single point, one can deliver a high dose of radiation at the intersection of those beams and decrease the dose to the surrounding tissue (early 1900s)
    - In the 1940s, stabilizing head frames were developed. This made the head an ideal target for radiosurgery
  - Lars Leksell developed a technique in 1951 which was later developed into the Gamma Knife
  - This was first used clinically in 1968
How Do We Immobilize the Spine like the Skull?

- Traditional cradles used in radiation do not provide enough immobilization
- Very difficult to fix the spine using frame technology
  - No reliable bony structure for fixation
- BodyFix for mid to lower thoracic and 5 point mask for cervical spine and upper thoracic

Verification of Positioning / Localization

- Required since we do not have a fixed frame as we do with brain radiosurgery
- Unlike with cranial radiosurgery, the immobilization device is not fixed to the patient in between planning imaging and treatment
- This requires image-guided techniques (Image Guided Radiation Therapy or IGRT)

IGRT

- CT-on-rails
- Cone-beam CT
  - Elekta (kilovoltage)
  - Varian (kilovoltage)
  - Siemens (megavoltage)
- Other IGRT systems
  - Novalis
  - CyberKnife
  - Tomotherapy

“Six Degrees of Freedom” Tabletop Allows for Increased Accuracy

- Not only does the table account for x, y, and z position, but it also takes into account pitch, yaw, and roll
- Many different versions
- May include an infrared tracking system to verify patient position (table top)
- Advantages
  - Can account for up to 5 degrees of rotation, improved accuracy
- Disadvantages
  - Increased weight of the device means table cannot handle very obese patients
  - Table thickness (attenuation) may need to be accounted for during planning
What do we know about SRS for benign tumors? - VESTIBULAR SCHWANNOMA

Retrospective Data from Pittsburgh

- 313 patients
- Marginal tumor dose: 12-13 Gy
- Median follow-up: 2 years
- 6-year control: 98.6%
- Preservation of facial function: 100%
- Preservation of trigeminal nerve: 95.6%
- Unchanged hearing: 70.3%
- Preservation of useful hearing: 78.6%

Flickinger et al., IJROBP 2004

SRS versus Surgery

- Timone Hospital, Marseille, France
- Prospective comparison of functional outcome (110 surgical patients versus 97 GK SRS patients)
  - New facial weakness: 37% with surgery vs. 0% with GK
  - Functional deterioration: 39% with surgery vs. 9% with GK
  - Trigeminal nerve disturbance: 29% with surgery vs. 4% with GK
  - Preserved hearing: 37.5% with surgery vs. 70% with GK
  - No difference for tinnitus (40-55%), vertigo (63-68%), or imbalance (22-26%)

Regis et al., J Neurosurg 2002

What do we know about SRS for benign tumors? - MENINGIOMA
Retrospective Review of Imaging-diagnosed Meningioma

- University of Pittsburgh
- 219 patients treated with GK
- Dose: 14 Gy
- Tumor control: 93.2% at 5 and 10 years
- Tumor progression developed in 7 patients, but 2 of these were misdiagnosis

Flickinger et al., IJROBP 2003

SRS versus Surgery (Retrospective)

- Mayo Clinic
- Retrospective review of 198 patients (136 patients with surgical resection and 62 with GK)
- Mean marginal dose: 17.7 Gy
- Tumor recurrence: 11% for surgery vs. 2% for SRS; p<0.05
  – 42% had Simpson Gr I resection
  – PFS was the same for Gr I resection versus SRS
- Complications: 10% for SRS vs. 22% for surgery; p=0.05

Pollock et al., IJROBP 2003

Spine SRS Would Make Sense for Benign Tumors

- Doses used are less than we often use for single fraction/session metastatic disease
  – 12-14 Gy for benign versus 16-24 Gy for metastatic/malignant tumors
- Conventional RT is typically given over 6 weeks
  – Logistical advantage for single fraction SRS
- Long term control has been demonstrated by SRS in the brain
  – So why not spine?

Data – Earlier Reports from Pittsburgh

- Gerszten et al. (Neurosurgery 2008):

<table>
<thead>
<tr>
<th>TABLE 3: Characteristics of lesions</th>
<th>No. of lesions (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level</td>
<td></td>
</tr>
<tr>
<td>Craniocervical</td>
<td>45 (50)</td>
</tr>
<tr>
<td>Thoracic</td>
<td>5 (7)</td>
</tr>
<tr>
<td>Lumbar</td>
<td>19 (26)</td>
</tr>
<tr>
<td>Sacral</td>
<td>6 (8)</td>
</tr>
<tr>
<td>Histology</td>
<td></td>
</tr>
<tr>
<td>Malignant</td>
<td>13 (18)</td>
</tr>
<tr>
<td>Benign</td>
<td>31 (41)</td>
</tr>
<tr>
<td>Neurofibroma</td>
<td>22 (24)</td>
</tr>
</tbody>
</table>

Gerszten et al. (Neurosurgery 2008)

- Dose: 15 to 25 Gy using Cyberknife

Representative Case from Gerszten et al.
Gerszten et al. (Neurosurgery 2008)

- Results
  - Long-term pain relief in 73%
  - Long-term radiographic control in all cases
  - Three patients developed myelopathy
    - 5-13 mo after radiosurgery
    - All in cervical spinal cord
    - Volume getting 8 Gy or more was 0.02 cc or less
- Conclusion: Longer follow-up needed

Georgetown Experience

- Gagnon et al. (Neurosurgery 2009)
  - 200 patients treated from 2002 to 2006
  - Patients were treated with multisession SRS using Cyberknife
  - 36 patients had benign disease

Georgetown Experience

- Mean pain decreased from 40.1 to 26.6 over 4 year period
- SF-12 show no change
- Mental component significantly higher suggestion improvement in quality of life
- There was no difference in improvement in malignant disease versus benign disease
- No myelitis noted
- Long-term effects included wound breakdown in 1 and vertebral body fractures in 2

Pittsburgh Experience with Using Synergy-S with CBCT

- Gerszten et al. (J Neurosurg 2012)
  - 45 consecutive patients with schwannoma, neurofibroma, and meningioma (ganglioglioma, aneurysmal bone cyst, and giant cell tumor)
  - CBCT technique was used (in their first series, they were treated with Cyberknife)
  - Median dose 16 Gy (range: 12-24)
  - Median f/u of 32 mo, no spinal cord or cauda equina toxicity was noted
  - 15 out of 19 patients had improvement in pain
  - Conclusion: Good safety profile and improvement of pain in some

Italian Experience

- Marchetti et al. (Acta Neurochir 2013)
  - 18 patients with 21 lesions with medium to long-term follow-up
    - 11 meningiomas, 9 schwannomas, and 1 neurofibroma
    - Cyberknife
    - 11 lesions had single session SRS, the rest received 4-6 sessions with dose ranging from 18.5 to 26 Gy
    - None developed progression
    - No long-term toxicity noted
Stanford Experience

- Sachdev et al. (Neurosurgery 2011)
  - 87 patients with 103 benign tumors (32 meningiomas, 24 neurofibromas, 47 schwannomas)
  - Treatment was delivered in 1-5 sessions
  - Dose was 19.4 Gy (range: 14-30 Gy)

Stanford Experience

- 59% were stable, 40% decreased in size, and a single tumor (1%) increased in size
- 91%, 67%, and 86% of meningiomas, neurofibromas, and schwannomas, respectively, were symptomatically stable to improved at last follow-up
- One complication: One patient with myelitis who had shrinkage of tumor, stabilized on corticosteroids
  - Pt treated to 24 Gy in 3 fractions, 4.7 cc spinal cord got over 8 Gy, 0.1 cc got over 27 Gy, max dose was 29.9 Gy

Case Example

- 30 yo with NF1
  - C1-2 neurofibroma s/p resection in 2009
  - Recurred in 2010, underwent re-resection
  - Recurred in 2011, underwent re-resection
  - Given history of recurrence and residual disease on re-resection, recommendation was for SRS
    - Pt received 12 Gy in 1 fx
  - Procedure complicated by pain flare relieved on Medrol Dose Pack

Taken from Marchetti et al. (Acta Neurochir 2013)
MRI 2 years later

Read as stable

Cleveland Clinic Multidisciplinary Tumor Board

- Meets once every 1-2 weeks
- Discuss cases
- For benign tumors, in general we favor surgical resection due to good prognosis of many of these patients
- Consider spine SRS in cases where surgery is not feasible, patient refuses surgery, disease recurrent despite prior surgery/radiation, or patient has comorbidities limiting overall survival (long-term toxicities become less a concern)

Spine SRS

- Advantages
  - Good control (similar to brain)
  - Non-invasive
  - Delivery is quicker than conventional RT
  - Pain relief is high post SRS
- Disadvantage
  - Despite studies, limited understanding of long-term risks
  - Myelopathy has been seen in other studies
  - Secondary malignancy may be a concern
  - Excellent results with surgical resection

Conclusion

- Spine SRS is effective in treating benign disease, specifically meningiomas, neurofibromas, and schwannomas
- Consider fractionated SRS for large tumors or tumors with extensive epidural disease (where cord tolerance limits dose to the tumor)
- Longer follow-up is needed to demonstrate safety