Radiosurgery for Skull Base Indications
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SCPMG

“Skull Base” Surgery
- Characterized by location along inferior and medial aspect of cranial fossae
- Often requires specialized approaches to remove bone to minimize need for brain retraction
  - Maximize exposure to tumor and normal structures
  - Minimize risk of damage to brain, nerves and vascular structures
  - Maximize likelihood of gross total resection

Pioneers of Skull Base
- Yasargil
- Kawase
- Parkinson
- Sekhar
- Dolenc
- House
- Spetzler
- Rhoton
- Koos
- Samii
- Al-Mefty

Skull Base Pathologies
- Meningioma
- Schwannoma
- Chordoma/Chondrosarcoma
- Hemangiopericytoma
- Malignant disease

Reports of outcomes from Skull Base approaches
- Few papers with much more than anecdotal or case report series.
- Preservation of cranial nerves – erratically reported
- Likelihood of gross total resection
- Long term control rates

The reality
- High morbidity
- High likelihood of subtotal resection
- Physical constraints of surgery from standpoint of neurological preservation and QOL
Meningiomas

- **Origin is arachnoid cap cell.**
- **Typical locations along skull base.**

**Typical locations along skull base:**

- **Incidence of 2.3 to 4.5/100,000 annually:** KP incidence of 80-160/year.
- **2:1 Female to Male ratio.**
- **Peak incidence in 60s.**
- **WHO classification:**
  - **1:** 80%
  - **2:** 15-20%
  - **3:** 1-5%
- **Disease control following surgery correlates with extent of resection.**
- **Really?**

Modern Series of Extent of Resection

- **More modern data from UCSF regarding extent of resection and tumor control.**

Scoring extent of resection

<table>
<thead>
<tr>
<th>Simpson Grade</th>
<th>Completeness of Resection</th>
<th>10-year Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade I</td>
<td>complete removal including resection of underlying bone and associated dura</td>
<td>9%</td>
</tr>
<tr>
<td>Grade II</td>
<td>complete removal + coagulation of dural attachment</td>
<td>19%</td>
</tr>
<tr>
<td>Grade III</td>
<td>complete removal w/o resection of dura or coagulation</td>
<td>29%</td>
</tr>
<tr>
<td>Grade IV</td>
<td>subtotal resection</td>
<td>40%</td>
</tr>
</tbody>
</table>

Control of Grade 1 Meningiomas

- **Shugrue, J Neurosurg 113:1029–1035, 2010.**

Long-term surgical outcome and biological prognostic factors in patients with skull base meningiomas

- **Clonal analysis:**
  - **CTE:**
  - **CTE with ETF:**
  - **ETF with ETF:**
  - **p<0.01**

- **J Neurosurg: Volume 114 / May 2011**
Clinical reports for cavernous sinus meningiomas

<table>
<thead>
<tr>
<th>Series</th>
<th>N</th>
<th>GTR</th>
<th>Morbidity</th>
<th>Fatalities</th>
</tr>
</thead>
<tbody>
<tr>
<td>DeMonte 1994</td>
<td>38</td>
<td>76%</td>
<td>8%</td>
<td>7.9%</td>
</tr>
<tr>
<td>Cusimano 1995</td>
<td>89</td>
<td>66%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DeJesus 1996</td>
<td>19</td>
<td>67%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Knosp 1996</td>
<td>29</td>
<td>21%</td>
<td>41%</td>
<td>0</td>
</tr>
<tr>
<td>O'Sullivan 1997</td>
<td>39</td>
<td>21%</td>
<td>12.8% homiparesisi, 12% cranial nerve deficits</td>
<td>0</td>
</tr>
</tbody>
</table>

Surgical Reports Petroclival Meningiomas

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>No. of Patients</th>
<th>Mortality (%)</th>
<th>CN Deficits (%)</th>
<th>GTR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sptot et al. 1991</td>
<td>19</td>
<td>0</td>
<td>39</td>
<td>78</td>
</tr>
<tr>
<td>Broek et al. 1992</td>
<td>33</td>
<td>9</td>
<td>76</td>
<td>79</td>
</tr>
<tr>
<td>Couldwell et al. 1996</td>
<td>109</td>
<td>3.7</td>
<td>33</td>
<td>69</td>
</tr>
<tr>
<td>Roberti et al. 2001</td>
<td>110</td>
<td>0.3</td>
<td>47</td>
<td>45</td>
</tr>
<tr>
<td>Litte et al. 2005</td>
<td>137</td>
<td>0.6</td>
<td>23</td>
<td>40</td>
</tr>
<tr>
<td>Park et al. 2006</td>
<td>49</td>
<td>2</td>
<td>38.6</td>
<td>20</td>
</tr>
<tr>
<td>Natrajan et al. 2007</td>
<td>150</td>
<td>0</td>
<td>20.3</td>
<td>32</td>
</tr>
<tr>
<td>Present study</td>
<td>50</td>
<td>0</td>
<td>32</td>
<td>28</td>
</tr>
</tbody>
</table>


Reality
- Hydrocephalus: 5.9%
  - Neurosurg Focus, 2011 May;30(5):E9
- Cranial nerve deficits
- Paresis
- Medical complications
- Fatality

Radiosurgery
- Developed by Leksell in 1950’s
- Currently practiced with a variety of devices employing similar treatment principles
- Classically defined as single session high conformity, high precision delivery of radiation energy.
- Now includes both single and fractionated dose delivery with high conformality

Geometric Superposition
- Dose divided equally among multiple beams (or arcs) in 3D
- Dose to a point is proportional to the number of beams illuminating it (fraction of time)
- Rapid dose fall off
- Fall off less rapid as beam size increases, leads to limited beam/target size, 3-5 cm diameter for cns targets.
- IMPORTANT that beams all converge on a point = target.
- Most commonly used method.

Early Radiosurgery
- Results not so good!
  - Poor imaging
    - CT
  - Poor understanding of dose
    - Excessive dose (>15 Gy to margin)
  - Poor treatment planning
    - 2D
    - Complex
  - Poor equipment
The KULA

Modern Practice of Radiosurgery
- Product of 5 decades of development
- Hundreds of thousands of treated patients.
- Since 1989, 663 radiosurgery manuscripts on radiosurgery treatment of meningiomas
- Since 1979, 687 articles related to radiosurgery for acoustic neuroma.
- A mainstay treatment.

SRS-FSR as a stand-alone or adjuvant
- Use of SRS as a primary means of definitive control of skull base tumors

Common Criticisms of SRS
- Questionable tumor control, does not get rid of tumor
- Will not improve symptoms
- May cause second tumor or transform tumor into cancer

Indications
- Indications for skull base tumors may include
  - Meningioma
  - Schwannoma
  - Metastatic
  - Chordoma
  - Paraganglioma
  - Hemangiopericytoma
  - Chondrosarcoma

Radiosurgery
- We always cover 100% of the tumor
- Extent of resection not an issue.
Three fold effect of SRS
- Direct tumor killing via apoptotic mechanisms
- Effects on mitotic mechanisms
- Effects on blood supply to tumor

Cranial Nerve Function
- General somatic efferents
  - Very radioresistant
- General somatic afferents
  - Radioresistant
- Special Sensory Nerves – Special Somatic Afferents
  - Poorly tolerant of radiation
- Special Visceral Afferents
  - Little data – likely intermediate sensitivity

Cases
- Yamamoto
- Rocio Barrios
- Acoustic neuroma cases
  - mengel
  - Carson 9755071

Patient AY
- 65 yo male with some gait instability.
- Full time working

Patient RB
- 29 yo female, pregnant with facial numbness
A Comparative Study of Stereotactic Radiosurgery, Hypofractionated, and Fractionated Stereotactic Radiotherapy in the Treatment of Skull Base Meningioma Series

**Table 2. Radiographic Tumor Control and Clinical Response to Treatment**

<table>
<thead>
<tr>
<th></th>
<th>SRS</th>
<th>IMRT</th>
<th>FSR</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%)</td>
<td>81</td>
<td>121</td>
<td>114</td>
<td></td>
</tr>
</tbody>
</table>

Radiographic tumor control in all patients

Tumor size at last follow-up:

- SRS: 6
- IMRT: 4 (1)
- FSR: 4 (1)

Failure:

- SRS: 12 (4)
- IMRT: 8 (2)
- FSR: 1 (1)

Clinical follow-up:

- SRS: 16 (4)
- IMRT: 10 (2)
- FSR: 8 (1)

Overall survival:

- SRS: 8 (4)
- IMRT: 6 (3)
- FSR: 2 (1)

2y radiographic tumor control:

- SRS: 8 (4)
- IMRT: 6 (3)
- FSR: 2 (1)

**Overall Survival**

Han et al Am J Clin Oncol (in press)

**References**

<table>
<thead>
<tr>
<th>Reference</th>
<th>Median Tumor Follow-up</th>
<th>Median Tumor Control</th>
<th>Median Tumor Control</th>
<th>Median Tumor Follow-up</th>
<th>Median Tumor Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>SRS</td>
<td>85%</td>
<td>95%</td>
<td>100%</td>
<td>13.5%</td>
<td>100%</td>
</tr>
<tr>
<td>IMRT</td>
<td>85%</td>
<td>95%</td>
<td>100%</td>
<td>13.5%</td>
<td>100%</td>
</tr>
<tr>
<td>FSR</td>
<td>85%</td>
<td>95%</td>
<td>100%</td>
<td>13.5%</td>
<td>100%</td>
</tr>
</tbody>
</table>

**KP-LAMC SRS-FSR Skull Base Meningioma Series**

- Progression Free Survival
- Han et al Am J Clin Oncol (in press)
Radiosurgery results for meningioma versus surgical results

- There has been no prospective randomized trial
- However, multiple retrospective studies have consistently shown that SRS yields local control similar to Simpson Grade 1 resection with low procedural morbidity and complications rates.

Cost

<table>
<thead>
<tr>
<th></th>
<th>Microsurgery</th>
<th>LINAC Radiosurgery</th>
<th>Gamma Knife Radiosurgery</th>
<th>Kruskal-Wallis Anova, p-value</th>
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</thead>
<tbody>
<tr>
<td>Initial treatment costs</td>
<td>12,280</td>
<td>1,047</td>
<td>2,912</td>
<td>0.024</td>
</tr>
<tr>
<td>Relative to microsurgery</td>
<td>100</td>
<td>17</td>
<td>20</td>
<td>0.176</td>
</tr>
<tr>
<td>Follow-up costs</td>
<td>2,641</td>
<td>1,514</td>
<td>1,555</td>
<td>0.120</td>
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<tr>
<td>General practitioner</td>
<td>75</td>
<td>65</td>
<td>163</td>
<td>0.312</td>
</tr>
<tr>
<td>Medical specialist</td>
<td>538</td>
<td>291</td>
<td>410</td>
<td>0.072</td>
</tr>
<tr>
<td>Physician assistant</td>
<td>344</td>
<td>222</td>
<td>207</td>
<td>0.029</td>
</tr>
<tr>
<td>Social worker</td>
<td>26</td>
<td>0</td>
<td>17</td>
<td>0.075</td>
</tr>
<tr>
<td>Company physician</td>
<td>166</td>
<td>96</td>
<td>62</td>
<td>0.026</td>
</tr>
<tr>
<td>Medical imaging services</td>
<td>540</td>
<td>340</td>
<td>540</td>
<td>0.531</td>
</tr>
<tr>
<td>Hospital stay</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1.000</td>
</tr>
<tr>
<td>Medications</td>
<td>126</td>
<td>299</td>
<td>172</td>
<td>0.308</td>
</tr>
<tr>
<td>Medical aid</td>
<td>6</td>
<td>11</td>
<td>3</td>
<td>0.592</td>
</tr>
<tr>
<td>Relative to microsurgery</td>
<td>100</td>
<td>74</td>
<td>76</td>
<td>0.000</td>
</tr>
<tr>
<td>Total costs</td>
<td>14,329</td>
<td>3,900</td>
<td>3,966</td>
<td>0.000</td>
</tr>
<tr>
<td>Relative to microsurgery</td>
<td>100</td>
<td>74</td>
<td>76</td>
<td>0.000</td>
</tr>
</tbody>
</table>

When to operate

- Local mass effect – e.g. hydrocephalus, myelopathy, peritumoral edema.
- Not cranial nerve deficits!
- Easily accessible lesion - Convexity
- Diagnosis: eg question of atypical or other pathology.
- Young age?
- Hydrocephalus
- Goals of Operating: Palliation

Novel Treatment for Meningiomas

- Somatostatin analogues
- Avastin
- Hormonal therapies
- Hydroxyurea

Cranial nerve schwannomas

- Classic surgical cases
- Also, given discrete margins has been a classic radiosurgery target.
Sometimes surgery is needed

- Non-skull base approach.
- Staged procedure – Retrosigmoid, Pterional Extradural.
- No deficit with exception of trigeminal dysfunction.

Observation

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Follow-Up (mo)</th>
<th>Growth Rate (mm/yr)</th>
<th>Failure Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sperber et al. 2019</td>
<td>322</td>
<td>43 (12-146)</td>
<td>1.1</td>
<td>4.4</td>
</tr>
<tr>
<td>Bakker et al. 2008</td>
<td>384</td>
<td>NA (12-108)</td>
<td>1.15</td>
<td>NA</td>
</tr>
<tr>
<td>Godfrey et al. 2009</td>
<td>70</td>
<td>46 (11-73)</td>
<td>0.45</td>
<td>NA</td>
</tr>
<tr>
<td>Nalluri et al. 2008</td>
<td>201</td>
<td>35 (1-193)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Fossi et al. 2008</td>
<td>123</td>
<td>56 (6-182)</td>
<td>0.3</td>
<td>NA</td>
</tr>
<tr>
<td>Hjort et al. 2008</td>
<td>72</td>
<td>121 (85-271)</td>
<td>1</td>
<td>NA</td>
</tr>
<tr>
<td>Stenstrom et al. 2008</td>
<td>636</td>
<td>47 (4-137)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Roat et al. 2004</td>
<td>72</td>
<td>80 (52-234)</td>
<td>1</td>
<td>3.1</td>
</tr>
<tr>
<td>Hoist et al. 2001</td>
<td>102</td>
<td>29 (6-120)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Walsh et al. 2000</td>
<td>72</td>
<td>40 (12-194)</td>
<td>1.42</td>
<td>4.2</td>
</tr>
</tbody>
</table>

Microsurgery

QOL

- Pollock, Neurosurgery VOLUME 59 | NUMBER 1 | JULY 2006
- Overall superior QOL scores when measured with standardized tests.
Novel Treatments for Acoustics

- Avastin – bevacizumab
- VEGF
- Trastuzumab
- ERBB2 inhibitor
- Erlotinib
- EGFR
- Lapatinib
- EGFR / HER2

Cost

- Surgery: $23,788
- Radiosurgery: $16,413

The wisdom of crowds?

- Patel S, Nuño M, Mukherjee D, Nosova K, Lad SP, Boakye M, Black KL, Patil CG.
- Stereotactic radiosurgery for vestibular schwannomas: a survey of current practice patterns of neurotologists.
- German MA, Zandouz S, Sina MK, Ziai K, Djalilian HR.

Chordoma

- A rare histologically benign tumor of the notochordal remanants.
Chordoma

- New molecular targeted therapies
- Tyrosine receptor kinase inhibitors
- Imatinib
- Dasatinib

Towards an integrated approach

- Recognize that limitations of tumor control
  - ARE related to the biology of the tumor,
  - NOT the technique of treatment
- Recognize that these are typically benign disease processes.
- QOL needs to be a paramount consideration on equal footing to oncologic extent of resection.
- Malignant tumors will require multimodality approaches
- Promise of molecular targeted medicine

Le Corbusier

- ... Man's stock of tools marks out the stages of civilization, the stone age, the bronze age, the iron age. Tools are the result of successive improvement; the effort of all generations is embodied in them. This too is the direct and immediate expression of progress; it gives man essential assistance and essential freedom also. We throw the out-of-date tool on the scrap-heap: the carbine, the culverin, the growler and the old locomotive. The action is a manifestation of health, of moral health, of morale also; it is not right that we should produce bad things because of a bad tool; nor is it right that we should waste our energy, our health and our courage because of a bad tool; it must be thrown away and replaced.

Where we must go

Follow-up and Referrals

- Please contact our clinical coordinator for radiosurgery patients who have been lost to our follow-up
- Ailene Rigoroso 323-783-1069
- Or e-mail me at Joseph.C.Chen@KP.org
Thank You