Benign Brain Tumors and the Role of Radiation Therapy – Radiosurgery and Protons

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Financial Disclosures

• None currently – 3 years ago was a speaker for Elekta (Gamma Knife).

Warnings

• I only treat CNS disease so I am very CNS focused.
• I wish insurance companies would be self consistent.
• This talk is designed to inspired critical thinking about what we do. (In benign brain tumors – we don’t have randomized trials.)
Survey

• With a show of hands – how many would treat a 55 year old with 6 sub-centimeter brain metastases from Lung cancer with WBI with hippocampal sparing?
Survey

• With a show of hands – how many would send an 8 year old child with a Grade III anaplastic astrocytoma for Proton therapy?
There are no randomized trials to show that either of those scenarios would be better then if they were treated to standard fractioned photon therapy.
What are the Benign Tumors?

• Acoustic neuromas (Vestibular schwannoma) (~7,000/yr US)
• Pituitary adenoma (secreting and non-secreting) (~10,000/yr US)
• Meningioma (~26,000/yr US)
• Craniopharyngioma (~700/yr US)

Bonus – Arteriovenous Malformation (AVM’s)

Incidence from CBTRUS 2004-2008
Why are Benign Brain Tumors a Challenge to Treat?

- About 50,000 cases per year in US.
- Overwhelming majority of tumors are managed by surgery.
- These are generally not diseases that kill patients.
- These are diseases that significantly impact Quality of Life.
- The toxicity of treatment must be included in the treatment decision.
Stereotactic Radiosurgery/Radiotherapy in One Slide

- Well Defined Target
- Patient Immobilization/Localization
- Rapid Dose Drop Off
What is a proton?

- Radiation therapy most often consists of photons or “x-rays”
- Protons are a heavy particle
  - Strip electrons from hydrogen gas
- Accelerate protons to very high speed
  - The greater the speed the deeper the penetration
  - 230 MeV - 32cm depth
  - ~ 2/3rds the speed of light
SCCA/Procure Proton Therapy Center

Beam Line
SCCA/Procure Proton Therapy Center
Proton physics: Bragg peak

Energy loss is small and constant until the end of the proton range
Physical advantage

15MV Photons vs SOBP Protons

Ideal Dose Distribution

Relative Depth Dose [%]

Depth [cm]
Comparison – 3D/IMRT/Proton
My Treatment Algorithm

• Small Tumors with Well defined Edges or Deep – SRS or SRT
• Large Tumors or Treatment Volumes – Protons or IMRT
Vestibular Schwannoma

- Benign Tumor of the 8th Nerve.
- Slow growing.
- Options – expectant management, surgery, fractionated radiation, or radiosurgery.
- Symptoms – hearing loss, balance problems, facial weakness, facial pain/numbness.
- Side effects of treatment
  - Loss of hearing
  - Balance problems
  - Facial weakness
  - Facial pain
  - Headaches
Vestibular Schwannoma

- Small tumors
  - Watch
  - Surgery
  - Radiation

- Medium Tumors/Growing Asymptomatic
  - Surgery
  - Radiation

- Large Tumors
  - Surgery +/- Radiation
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* All patients underwent GCS. Abbreviations: ID = Identification; NA = not available.
Acoustic Neuroma

• 55 yo male presented with left jaw pain.
• Incidental left CP angle tumor identified. Subjective decrease in hearing on the left.
• Underwent Gamma knife Sept 2005.
  • 12 Gy to the 50% isodose curve using 10 isocenters.
Follow Up

2006

2007

2008

2009
HEARING PRESERVATION AFTER GAMMA KNIFE RADIOSURGERY FOR VESTIBULAR SCHWANNOMAS PRESENTING WITH HIGH-LEVEL HEARING

OBJECTIVE: The aim of this study was to evaluate long-term hearing preservation after gamma knife radiosurgery (GKS) for vestibular schwannomas in patients with initially normal or subnormal hearing (Gardner-Robertson Class 1) and to determine the predictive factors for functional hearing preservation.

METHODS: Since July 1992, more than 2053 vestibular schwannomas have been treated by GKS and followed at the Timone University Hospital, Marseille. A minimum of 3 years of follow-up (range, 3–11 years; median, 48 months) is available for 74 patients (without neurofibromatosis type 2 or previous surgery) with Gardner-Robertson Class 1 hearing.

RESULTS: The average age of the patients was 47.5 years (range, 17–76 years). The number of tumors in Koos Stage I was 8, the average number in Stage II was 21, the average number in Stage III was 43, and the average number in Stage IV was 2. The median number of isocenters was 8 (range, 2–45), and the median marginal dose was 12 Gy (range, 9–13 Gy). At the time of the last follow-up evaluation, 78.4% of the patients had preserved functional hearing. Tumor control was achieved in 93% of the cases. The probability of preserving functional hearing was higher in patients who had an initial symptom other than hearing decrease (91.1%), in patients younger than 50 years (83.7%), and in those treated with a dose to the cochlea of less than 4 Gy (90.9%).

CONCLUSION: This study shows that the probability of preserving functional hearing in the long term after GKS for patients presenting with unilateral vestibular schwannomas is very high. The positive predictive factors appear to be young age, an initial symptom other than hearing decrease, and a low dose to the cochlea.

KEYWORDS: Cochlear dose, Hearing preservation, Gamma knife, Quality of life, Vestibular schwannoma
GKS Treatment

A: Multicentric dose planning at 12 Gy margin, relying on multimodal imaging with bone CT and high resolution MRI.

B and C: Parameters related dose plan (Dose to cochlea, figure B) and lesion morphology (Total tumor and Intracanalicular tumor, figure C).

FIGURE 1. Fusion imaging with computed tomographic and magnetic resonance imaging scans provides accurate dose planning information for the treatment of vestibular schwannomas with gamma knife radiosurgery (GKS). We measure numerous parameters for the preservation of subnormal hearing (Gardner-Robertson [GR] Class 1) after GKS.
FIGURE 2. Graph showing the probability of conservation of functional hearing (GR Class 1 and 2) in the long term. In more than 70% of patients, the rate of hearing decrease reaches a plateau after 7 years.
Pituitary Adenoma

- Benign Tumor of the pituitary gland
- Non-secreting – normal hormones
- Secreting – overproduction of hormones
  - Growth Hormone
  - ACTH.
- Surgery is first line
- Those that need radiation tend to be worse biologically.
- Patient can rarely die from pituitary tumors – mainly due to continued over productions of hormones.
### Pituitary Directed Stereotactic Radiosurgery (14-24 Gy in single fraction)

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Pituitary Tumors

- Good local control for both secreting and non-secreting adenomas (Dose: 15-36 Gy)
  - 65% have tumor regression
- Variable response to hormone levels
  - GH: 65% had decrease by 6 months and 77% by 12 months (20% normalized) (ILGF normalization less ~ 30-40%)
  - PRL: 46% had decreased by 6 months and 64% by 12 months (0% normalized)
  - Cortisol: normalized in 66% of patients in 6-12 months.
- Deficiency in ~20% for LH/FSH, TSH and ~10% for ACTH and GH
68 yo with left eye pain was found to have a pituitary mass (hormones ok). Grew over time. Due to cardiac history was not a surgical candidate. Treated with Gamma Knife (15 Gy to the 50% isodose surface. Optic Chiasm max point dose – 7.7 Gy.)
pituitary Tumor - SRS
Pituitary Tumor - SRS
pituitary Tumor - Protons
Physical advantage

15MV Photons vs SOBP Protons

Ideal Dose Distribution

Relative Depth Dose [%]
I meningiomas

Mainly benign tumors of the meninges.
Standard has been surgery – radiation reserved for tumors that recur or are not resectable without significant risk of morbidity.
Grade III – anaplastic meningioma have a median survival of about 3 years.
Multiply recurrent tumors put patients as risk for metastatic disease.
Long-term Tumor Control of Benign Intracranial Meningiomas After Radiosurgery in a Series of 4565 Patients

**BACKGROUND:** Radiosurgery is the main alternative to microsurgical resection for benign meningiomas.

**OBJECTIVE:** To assess the long-term efficacy and safety of radiosurgery for meningiomas with respect to tumor growth and prevention of associated neurological deterioration. Medium- to long-term outcomes have been widely reported, but no large multicenter series with long-term follow-up have been published.

**METHODS:** From 15 participating centers, we performed a retrospective observational analysis of 4565 consecutive patients harboring 5300 benign meningiomas. All were treated with Gamma Knife radiosurgery at least 5 years before assessment for this study. Clinical and imaging data were retrieved from each center and uniformly entered into a database by 1 author (A.S.).

**RESULTS:** Median tumor volume was 4.8 cm³, and median dose to tumor margin was 14 Gy. All tumors with imaging follow-up < 24 months were excluded. Detailed results from 3768 meningiomas (71%) were analyzed. Median imaging follow-up was 63 months. The volume of treated tumors decreased in 2187 lesions (58%), remained unchanged in 1300 lesions (34.5%), and increased in 281 lesions (7.5%), giving a control rate of 92.5%. Only 84 (2.2%) enlarging tumors required further treatment. Five- and 10-year progression-free survival rates were 95.2% and 88.6%, respectively. Tumor control was higher for imaging defined tumors vs grade I meningiomas (P < .001), for female vs male patients (P < .001), for sporadic vs multiple meningiomas (P < .001), and for skull base vs convexity tumors (P < .001). Permanent morbidity rate was 6.6% at the last follow-up.

**CONCLUSION:** Radiosurgery is a safe and effective method for treating benign meningiomas even in the medium to long term.

**KEY WORDS:** Control rate, Follow-up, Meningiomas, Multicenter study, Radiosurgery
Meningioma – Sub-totally resected – Multi-Session GK
Meningioma – Sub-totally resected – 18 Gy in 3 fractions
Meningioma – Sub-totally resected – 18 Gy in 3 fractions

3 year follow up
Meningioma – Sub-totally resected – 18 Gy in 3 fractions

3 year follow up
Meningiomatosis - Protons

5580 cGyE in 31 fractions
Meningiomatosis - Protons

Pre 1 Year Post

5580 cGyE in 31 fractions
Meningiomatosis - Protons

5580 cGyE in 31 fractions
Meningiomatosis - Protons

5580 cGyE in 31 fractions
Meningiomatosis - Protons
## Meningiomatosis - Protons

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<td>Corrections to MRI/CT fusion requested</td>
</tr>
<tr>
<td></td>
<td>Hippocampal Contouring</td>
<td>≤ 2 mm deviation using the Hausdorff distance⁶</td>
<td>&gt; 2, ≤ 7 mm deviation using the Hausdorff distance⁶</td>
<td>&gt; 7 mm deviation using the Hausdorff distance⁶</td>
</tr>
<tr>
<td>HA-WBRT IMRT Planning</td>
<td>PTV</td>
<td>D2% ≤ 37.5 Gy</td>
<td>D2% &gt; 37.5 Gy, ≤ 40 Gy</td>
<td>V30 &lt; 90%</td>
</tr>
<tr>
<td></td>
<td>Hippocampus</td>
<td>D100% ≤ 9 Gy Maximum dose ≤ 18 Gy</td>
<td>D100% ≤ 10 Gy Maximum dose ≤ 17 Gy</td>
<td>D100% &gt; 10 Gy Maximum dose &gt; 17 Gy</td>
</tr>
</tbody>
</table>
Raniopharyngioma

Benign brain tumor derived from pituitary gland embryonic tissue.

Bimodal distribution – young and 50-60’s.

Long-term risk of impacting STM (hippocampi) and pituitary function.
raniopharyngioma
raniopharyngioma – Multi-session

16 yo female
Resected craniopharyngioma 2006
Post-op lost all vision in her right eye and has had persistent 20/400 vision in the nasal portion of her left eye.
Pan-hypo pit.
Recurrence in 2010 adjacent to optic chiasm
Treatment options – XRT, Protons, Multi-Session
Gamma Knife
Treatement Accuracy 0.8, 0.3, 0.4, 0.3, 0.6)

20 Gy/5 fx/12 min per fx
Benign Tumors require a multi-disciplinary approach.

Goals of treatment must be to reduce complications and provide tumor control in a patient centric manner.

There are no randomized trials to clearly determine what is best. So 1st principal applies—less dose to less brain is better.

Trials are expensive – registries may be better option.

In the future – the “best” option will be defined by criteria/markers not even developed yet.
Stereotactic Radiosurgery for AVM’s
0.1% of population harbor brain AVM’s
50% present with hemorrhage, 20-25% with seizures.
Risk of hemorrhage 2-3% per year. Risk of mortality from first bleed is 10-30%. Survivors had a 10-20% chance of a permanent neurological deficit.

Olilvy et al., *Stroke*. 2001;32:1458-1471. AHA consensus statement
Complex AVM

Young Woman s/p IPH
Two attempts at Surgery and 1 with Embolization
Case 2 – AVM

[Image of an arteriovenous malformation (AVM)]
Case 2 – AVM
Case 2 – AVM
70-90% obliteration of AVM at three years. Fifty percent will be obliterated in 1 year. (Dose: 15-24 Gy)

- Pt’s still at risk of bleed until abnormality obliterated (2-4% each year).
- Large AVM’s may need to be done in a stage procedure (>3.5 cm).
- Pts followed with MRI at 6 months then 1, 2, and 3 years. When lesion gone on MRI, then angio is repeated.
Stereotactic Radiosurgery is effective treatment for AVMs less than 3 cm.
Risk profile dependent on volume and location.
Effectiveness is dose dependent.
Patient need long term follow up following radiation therapy.