Upfront Gamma Knife radiosurgery for Cushing’s disease and Acromegaly: A multicenter, international study.

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Disclosure

L. Dade Lunsford, MD, PhD - owns stocks of Elekta
Cushing’s disease (CD) and acromegaly, if left untreated may lead to significant systemic sequelae and even death.

**Established Treatments:**
- **Medical therapy** first choice
- Stereotactic radiosurgery (SRS)
- Postresection for residual or recurrent tumor

**Secretory adenoma**
- 1. ACTH-CD
- 2. GH-Acromegaly

**Drug therapy**
- Surgery
- SRS

**Goals of treatment**
- Tumor control
- Endocrine normalization

**Aim:** Initial Gamma Knife surgery (GKS) for select cases of Cushing’s disease and acromegaly
Methods: A retrospective study - Upfront GKS defined as patients with no prior h/o surgery or radiation for pituitary adenoma

- Cushing’s disease (CD) 21 patients
- Acromegaly patients 25
- High Surgical risk = 27
- Choice of treatment = 19
- Seven centers Total = 46 patients

Inclusion criteria:

- Clinical
- MRI tumor vol.
- Gamma plan or abc/2
- Complete Hormonal Profile
## Results: Characteristics in 46 patients

<table>
<thead>
<tr>
<th>Patients Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cushing's disease(21)</td>
</tr>
<tr>
<td>median age in years (range)</td>
<td>39 (14-79)</td>
</tr>
<tr>
<td>sex (female / male)</td>
<td>19:2</td>
</tr>
<tr>
<td>median tumor vol. in cc (range)</td>
<td>0.5 (0.01-1.7)</td>
</tr>
<tr>
<td>no. of macro adenomas (%)</td>
<td>4 (19)</td>
</tr>
<tr>
<td>no. of patients w/CS extension (%)</td>
<td>4 (19)</td>
</tr>
<tr>
<td>no. of patients w/suprasellar extension (%)</td>
<td>2 (5)</td>
</tr>
<tr>
<td>no. of patients w/pre-GKS hypopituitarism (%)</td>
<td>3 (14.3)</td>
</tr>
<tr>
<td>no. of patients w/pre-GKS visual deficits (%)</td>
<td>3 (14.3)</td>
</tr>
<tr>
<td>median imaging FU in mos. (range)</td>
<td>44 (3-180)</td>
</tr>
<tr>
<td>median endocrine FU in mos. (range)</td>
<td>63 (9-246)</td>
</tr>
</tbody>
</table>

*CS= cavernous sinus; FU= follow-up; mos.=months, w/= with*
Radiosurgical attributes of upfront GKS

- Median margin dose: 25 Gy
- Median 50% isodose

Hypopituitarism in 9 patients (19.6%) - median margin dose 30 Gy (range 16-35 Gy)

- Optic nerve: 6.2 Gy (range 1-12 Gy)
- Optic chiasm: 5 Gy (range 1-10 Gy)
- Optic tract: 4.5 Gy (range 1-8.5 Gy)

- GKS whole sella: 33%
- CD: 33%
- Acromegaly: 32%
Endocrine remission: overall 51% at median 69.5 months

The tumor secretory type, i.e. ACTH versus GH was seen as a significant factor (p=0.0005) in achieving a better remission rate.

Actuarial endocrine remission rate at 1, 2, 3, and 5 years in CD patients was 46%, 68%, 74% & 81%, respectively and in acromegaly was 4%, 8%, 17% & 28%, respectively.
Results: Outcome of 46 patients, none with radionecrosis

<table>
<thead>
<tr>
<th>Parameter</th>
<th>No. of patients (%)</th>
<th>Time in months (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tumor response</strong></td>
<td></td>
<td></td>
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<tr>
<td>Regression (≤ 20% tumor volume change)</td>
<td>28(61)</td>
<td>24(3-60)</td>
</tr>
<tr>
<td>Stability (within ± 20% tumor volume change)</td>
<td>18(39)</td>
<td>35.2(3-116)</td>
</tr>
<tr>
<td>Enlargement (≥ 20% tumor volume change)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td><strong>Clinical improvements</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discontinued anti-secretory Rx</td>
<td>5(11)</td>
<td></td>
</tr>
<tr>
<td>Started anti-secretory Rx</td>
<td>13(28.3%)</td>
<td></td>
</tr>
<tr>
<td><strong>Complications</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CN II palsy (optic)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>CN III palsy (oculomotor)</td>
<td>1(2.2)</td>
<td>36 (2nd GKS)</td>
</tr>
<tr>
<td>Hypopituitarism*</td>
<td>9(19.7)</td>
<td>32.5(6-63)</td>
</tr>
<tr>
<td>Thyroid deficiency</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Multi-hormonal deficiency</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Panhypopituitarism †</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Patient undergoing further surgery</td>
<td>8(17.4)</td>
<td>Surgery at 27, 48 Re-GKS 39.5 (21-96)</td>
</tr>
</tbody>
</table>

* [ 5 CD + 4 acromegaly], † CD
Discussion

- **Peter et al**
  - 135 (81 aged 60–69 years and 54 ≥ 70 years) patients undergoing endoscopic transsphenoidal surgery for pituitary tumor
  - Graded increase (7.4% Vs 18.5%) complication rates with increasing age

- **Castinetti et al**
  - 27 (out of total 76) patients treated upfront GKS for secretory pituitary adenoma
  - Remission rate was 40.7% mean FU of 102 months {50% with microadenomas Vs 33.3% with macroadenomas (P ≤ 0.05)}

- **Mehta et al & Lee et al**
  - Results of post resection GKS:
    - Lee studied 136 acromegaly patients remission rate of 65.4% at FU of 61.5 months.
    - Mehta studied 278 CD patients with remission rate of 64% at 10 years FU.

- **Current study**
  - Remission rate 51% overall, and 28% in acromegaly versus 81% CD (P ≤0.05).
  - Adenoma control 39% patients had a stable tumor size and 61% showed reduction
  - New hypopituitarism 19.6% and cranial nerve deficit 2.2%
Summary for Upfront GKS

Overall
Reasonable rate of tumor control &
Low rate of adverse radiation effects

Endocrine Remission rates
Faster & higher in CD than acromegaly

Longitudinal follow-up needed, though low rate of
• Hypopituitarism
• Recurrence

CD patients unwilling or unable to undergo resection

Limited role Acromegaly