Functional Neurosurgical Applications of Modern Precision Radiosurgery

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Disclosures

- Honorarium/Institutional Research Agreement from Varian
- Conflicts of interest to report:
  - None
Functional Neurosurgery

- Neurosurgical intervention when physiology is altered, but anatomy may or may not be normal.
- Historically, required thermal ablation or direction injection of injurious chemical (e.g., phenol or ethanol).
- Developed in parallel with the practice of stereotaxy.

First stereotaxic apparatus by Horsley, 1908 (not used in humans).
Brief History of Functional Radiosurgery

- **1951** – Introduction of SRS by *Leksell*
  - Original intended use was functional conditions (e.g. PD, psych disorder, chronic pain)
- **1958** – First described use of protons for fxnl SRS by *Larrson, Leksell & Rexed* (200Gy to anterior internal capsule)
- **1967** – *GammaKnife* introduced
  - Immediately in use for functional disorders
- **1998** – First described LINAC fxnl SRS (trigeminal neuralgia) by *De Salles et al*
- **2003** – *CyberKnife* first used for fxnl SRS (trigeminal neuralgia) by *Romanelli, Adler, et al.*
How relevant is functional radiosurgery?

- Recent study surveyed 66 centers in 34 countries worldwide on their utilization of Gamma Knife radiosurgery (GKRS) compared to potential indications
- Survey included functional indications
  - Trigeminal neuralgia
  - Medically refractory tremor
  - Epilepsy
  - Behavioral disorders
  - Mood disorders
Functional Radiosurgery

Under Utilized

Under Recognized

A significant variance was observed among regions regarding the role of GKRS for medically refractory essential or parkinsonian tremor. North American surveys estimated that 13% of patients with tremor were appropriate for treatment, compared with 6% estimated as appropriate in Asia and 7% in Europe.

Delivery of Functional Radiosurgery

Nearly all functional SRS cases are currently performed on Gamma Knife® Perfexion™, a linear accelerator with cones, or CyberKnife®.
Cone-based functional SRS on LINAC

- Cone-based SRS approaches associated with practical limitations to clinic workflow and require a specialized dose calculation system
- Patient-specific geometric QA (Winston-Lutz test) required immediately before procedure
- Additional quality assurance effort when cones are taken on and off
- High-profile accidents associated with cones
  - Evanston, Toulouse, etc
For those with LINACs, is there a better way?

- Robust targeting
- Reliable treatment delivery
- Maximal patient convenience and comfort
  - completely non-invasive (frameless)
  - expedited treatment time
Virtual Cone (VC) on the Edge™

- MLC-based (Virtual Cone) VMAT SRS developed by Dr. Richard Popple (UAB) in concert with VMS
  - Pre-calculated fixed modulation pattern VMAT plan, with static MLC leaves
- Pre-defined MLC control point sequence designed to create a 4 mm to 5 mm diameter dose distribution
- Model using standard dose calculation algorithm (AAA)
- Geometric QA (MLC Winston-Lutz) can be completed on a more flexible schedule
Virtual Cone MLC Aperture and Arc Geometry

- CW & CC arcs with collimator ±45 degrees
- 5 mm x 2.1 mm fixed MLC aperture
- Dose rate $\alpha \sin(\text{gantry angle})$
Comparison of Dose Profiles in Virtual Cone Using Dose $\propto \sin (\text{gantry})$ vs constant dose

Dose distribution for a virtual cone treatment plan having dose per degree a) proportional to sine of the gantry angle and b) constant. Displayed isodose lines correspond to 50% (yellow), 25% (green), and 10% (cyan) of the maximum dose.
Comparison of measured to calculated virtual cone dose profile

Mean ratio of film to TPS **1.03** (range 1.02 to 1.04). Mean offset between the measured and calculated dose in the film plane **0.3 mm**
Trigeminal Neuralgia

- Increasingly recognized as more common than previously thought
- Revised estimates of prevalence are 0.03 – 0.3%
- Conservatively 90000 in the United States
- Previously estimated at ~40000
Trigeminal Neuralgia (cont’d)

- Multiple micro-surgical and minimally invasive techniques to treat trigeminal neuralgia

Needle insertion into foramen ovale (Hartel’s technique)
### Trigeminal Neuralgia SRS Studies

#### Table 3  Selected studies using various SRS modalities and respective pain control and complication rates

<table>
<thead>
<tr>
<th>Modality</th>
<th>Publication</th>
<th>No. of patients</th>
<th>Dose (Gy)</th>
<th>Median follow-up (mo)</th>
<th>Pain control</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gamma Knife</td>
<td>Maesawa et al(^5) (2001)</td>
<td>220</td>
<td>80 (48.6%); range, 60-90</td>
<td>24.0</td>
<td>Pain relief at 1 y: 70.3%</td>
<td>Ipsilateral facial numbness: 10.2%</td>
</tr>
<tr>
<td></td>
<td>Kondziolka et al(^6) (2010)</td>
<td>503</td>
<td>80 (88%); range, 60-90</td>
<td>24.0</td>
<td>BNI I-III at 1 y: 80%; recurrence rate: 42.9%</td>
<td>Ipsilateral facial paresthesia: 10.5% Ipsilateral facial numbness: 10%</td>
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<tr>
<td></td>
<td>Lee et al (2015)(^23)</td>
<td>133</td>
<td>80 (all)</td>
<td>22.8</td>
<td>Recurrence rate: 31%</td>
<td></td>
</tr>
<tr>
<td>CyberKnife</td>
<td>Adler et al(^5) (2009)</td>
<td>46</td>
<td>73.5 (mean maximal)</td>
<td>14.7</td>
<td>Excellent or good patient-reported outcome: 72% 24%</td>
<td>Ipsilateral facial numbness: 15%</td>
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<td></td>
<td>Tang et al (2011)(^24)</td>
<td>14</td>
<td>80.5 (mean maximal)</td>
<td>20.4</td>
<td>Initial response: 92.8%</td>
<td>Ipsilateral facial numbness: 14.2%</td>
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<td>Lazzara et al (2013)(^25)</td>
<td>17</td>
<td>73.06 (mean)</td>
<td>5.0 (mean)</td>
<td>Initial partial or complete response: 86%</td>
<td>Dysesthesia or numbness: 11.8%</td>
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<td>Karam et al (2014)(^21)</td>
<td>25</td>
<td>64 (mean)</td>
<td>28.0</td>
<td>Freedom from severe pain (BNI IV-V): 72%</td>
<td>New facial numbness or pain: 28%</td>
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<tr>
<td>LINAC-based with</td>
<td>Goss et al(^12) (2003)</td>
<td>25</td>
<td>90</td>
<td>12.0</td>
<td>Excellent or good pain relief: 76% 24%</td>
<td>Ipsilateral facial numbness: 32%</td>
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<tr>
<td>flattening filter</td>
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<td></td>
<td>80</td>
<td>12.0</td>
<td>Complete or significant pain relief: 75%</td>
<td>Ipsilateral facial numbness: 10.7%</td>
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<td>Richards et al(^11) (2005)</td>
<td>28</td>
<td>80</td>
<td>12.0</td>
<td></td>
<td>Any degree of numbness: 49.7%</td>
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<td></td>
<td>Smith et al(^14) (2011)</td>
<td>169</td>
<td>90 (83.4%); range, 70-90</td>
<td>28.8</td>
<td>Excellent or good pain relief: 88.5%</td>
<td>New dysesthesia or hypoesthesia: 0%</td>
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<tr>
<td>LINAC-based, FFF</td>
<td>Current study</td>
<td>36</td>
<td>75 (median)</td>
<td>5.5 (mean)</td>
<td>Pain relief by first follow-up: 88.5%; medication-free pain relief: 15%</td>
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BNI, Barrow Neurological Institute pain score; CK, CyberKnife; FFF, flattening filter free; GK, Gamma Knife; LINAC, linear accelerator.
UAB Virtual Cone SRS for Trigeminal Neuralgia Trial (RAD 1501)

• **Stage I (Pilot at UAB Only, Single Institution)**
  - To determine the feasibility of frameless Virtual Cone trigeminal neuralgia radiosurgery at a single institution prior to multi-institutional enrollment.

• **Stage II (Multi-Institutional)**
  - To measure pain relief after Virtual Cone radiosurgery utilizing the Barrow Neurologic Institute Pain Intensity Score (BNI).

![Schema]

- Trigeminal Neuralgia
  - 80 Gy Virtual Cone Framed or Frameless
  - Assessments (1 year follow-up):
    - Toxicity (CTCAE v4)
    - BNI Pain Intensity Score
    - Patient satisfaction questionnaire
    - QOL (SF-36)
Successful VC SRS Trigeminal Nerve Ablation

75-Gy Left trigeminal nerve ablation for tumor associated pain (Left cavernous sinus tumor treated separately to 16 Gy)
UAD 1501 Trial Status

- Pilot targeted 20 patients, originally 10 frameless, 10 framed
  - Now treating all frameless
  - 25 accrued, 1 more enrolled, 1 more pending enrollment
  - Pace of accrual greatly increased with neurosurgeon engagement
- Plans to extend single-institutional phase of trial for additional accrual
- Search for multi-institutional partner narrowed to one of a few candidate institutions

- Results:
  - Pain relief consistent with previous literature reported rate
  - No unusual or unexpected toxicity
  - Patients pleased with ease and comfort of procedure
Essential & Parkinsonian Tremor

- Est. 10 million Americans with essential tremor
- Est 1-2 million with Parkinsonian tremor
- 25-55% are medication refractory
  - Of these, ~40% not surgical (deep brain stimulation, DBS) candidates
- Conservative estimate of possible tremor SRS candidates in United States
  - ~1 million
Radiosurgical Thalamotomy

- Lesion is usually placed at the ventral intermediate nucleus (VIM) of the contralateral thalamus
Efficacy of Radiosurgical Thalamotomy

A prospective single-blind study of Gamma Knife thalamotomy for tremor

ABSTRACT

Objective: To evaluate the safety and efficacy of unilateral Gamma Knife thalamotomy (GKT) for treatment of severe tremor with a prospective blinded assessment.

Methods: Fifty patients (mean age 74.5 years; 32 men) with severe refractory tremor (36 essential, 14 parkinsonian) were treated with unilateral GKT. Targeting of the ventral intermediate nucleus (Vim) was achieved with Leksell Gamma Knife with a single shot through a 4-mm collimator helmet. The prescription dose was 130 Gy. Neuropsychological assessments including a single-blinded video assessment of the tremor severity performed by a movement disorders neurologist from another center were performed before and 12 months after treatment. MRI follow-up occurred at 3, 6, and 12 months.

Results: The upper limb tremor score improved by 54.2% on the blinded assessment (p < 0.0001). All tremor components (rest, postural, and intention) were improved. Activities of daily living were improved by 72.2%. Cognitive functions remained unchanged. Following GKT, the median delay of improvement was 5.3 months (range 1-12 months). The only side effect was a transient hemiparesis associated with excessive edema around the thalamotomy in one patient.

Conclusion: This blinded prospective assessment demonstrates that unilateral GKT is a safe and efficient procedure for severe medically refractory tremor. Side effects were rare and transient in this study.

Classification of evidence: This study provides Class IV evidence that for patients with severe refractory tremor, GKT is well tolerated and effective in reducing tremor impairment.

Global score

Effect of treatment. The boxes extend from the first to third quartiles. The lines in the middle represent the medians. The whiskers go down to the smallest value and up to the largest. ***p < 0.001. After unilateral GK thalamotomy, there was a significant improvement in the upper limb tremor score whatever the item considered.
UAB RAD 1601 – Pilot Trial of Frameless Virtual Cone SRS Thalamotomy for Medically Refractory Tremor and Advanced Functional Connectivity Parcellation of the Thalamus

• **Primary objective:**
  • Determine the efficacy of frameless Virtual Cone radiosurgical thalamotomy for medically refractory tremor resulting from either essential tremor or tremor-dominant Parkinson’s Disease with the Fahn-Tolosa-Marin Tremor Rating Scale (FTMTRS) in patients who are not candidates for deep brain stimulation (DBS) or do not want DBS

• **Eligibility:**
  • Patients with medically refractory ET or tremor-dominant PD
  • >18 years old
  • no prior brain SRS or therapeutic brain RT
This trial will initially target enrollment of twenty patients at a single institution to confirm that all study procedures and assessments are feasible and safe.

### 4.0 PATIENT SELECTION CRITERIA

#### 4.1 Inclusion Criteria

- Identify 20 patients
- Medically refractory, non-DBS candidate

#### 4.2 Exclusion Criteria

- Assess baseline tremor/ADL score
- Acquire baseline imaging
- 130Gy Virtual Cone radiosurgical thalamotomy
- Clinical neurology: tremor/ADL assessment 3, 6, 12 mo
- MRI: immediately pre-tx, 2wks, 6 mo, 12 mo

### 6.2.2 Schedule of Imaging*

<table>
<thead>
<tr>
<th>Image Sequence</th>
<th>Pre-RS</th>
<th>2 weeks</th>
<th>6 months</th>
<th>12 months</th>
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<tbody>
<tr>
<td>T1 weighted image</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>T2 weighted image</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Diffusion Weighted Image</td>
<td>X</td>
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<td>X</td>
<td>X</td>
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<tr>
<td>Resting fMRI</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Task Based fMRI</td>
<td>X</td>
<td></td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>3T Novel Targeting Study (UAB)</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7T Novel Targeting Study (Auburn University)</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Automated stereotactic targeting

- **AP**: 1/4 of the AC–PC distance plus 1 mm anterior to the PC
- **Lat**: 1/2 the width of the 3rd ventricle plus 11 mm from the AC–PC line
- **Sup-Inf**: 2.5 mm superior to the AC–PC
- 130 Gy $D_{\text{max}}$ (65 Gy to 4.5-mm VC)
- 20% (26Gy) IDL line kept medial to IC
Scripted treatment planning

- 0.8 mm grid size
- 10 framework agent servers
- Calculation time
  - AAA 13.6 - 23.4 min
  - Acuros XB 13.6 (plan dose) – 14.8 min
  - Acuros XB 13.6 (field by field) – 2.8 min
- Soon: GPU acceleration for massively parallel computation
SRS thalamotomy plan (MPRAGE)
SRS thalamotomy plan (FGATIR)
FGATIR sequence on 3T and 7T

- FGATIR = Fast Gray Matter Acquisition T1 Inversion Recovery
- white-matter nulled sequence
- same acquisition as MPRAGE (different inversion time)
- allows for improved delineation of subcortical structures
  - specifically thalamus, striatum, GPe/GPi, RN, SNr)
  - enables seeing internal lamina of the GPi, fiber bundles from the IC piercing the striatum, and the boundaries of the STN
First Treated Essential Tremor Patient – 130Gy dmax to Left VIM of thalamus

Pre-tx MRI compared to 3mo post-tx MRI

In vivo dose delivery verification!
UAB 1601 Status

• Officially opened one year ago
  • 3 patient treated off protocol
  • Adjusted to include tremor dominant Parkinson’s

• Currently:
  • 15 patients treated and actively enrolling
RAD 1601 Current Results

FTM Scores by Patient

- Baseline
- Treatment
- 1 MO
- 3 MO
- 6 MO
- 12 MO

Scores:
- 1
- 4
- 5
- 6
- 7
- 8
- 9
- 10
- 12
Other potential applications we are exploring:

Radiosurgical Management of Intractable Pain in Terminal Cancer Patients
Pain in cancer patients

Patients undergoing cancer treatment: 33 – 59% significant disabling pain

Patients with advanced disease: 64 – 74% significant disabling pain

## Prevalence of pain among different types of cancer

<table>
<thead>
<tr>
<th>Type of cancer</th>
<th>Groups 2–4 % pain (95% CI)</th>
<th>No. of reports</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head/neck</td>
<td>70% (51% to 88%)</td>
<td>3</td>
<td>95</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>59% (44% to 74%)</td>
<td>9</td>
<td>564</td>
</tr>
<tr>
<td>Lung/bronchus</td>
<td>55% (44% to 67%)</td>
<td>7</td>
<td>1546</td>
</tr>
<tr>
<td>Breast</td>
<td>54% (44% to 64%)</td>
<td>7</td>
<td>420</td>
</tr>
<tr>
<td>Urogenital</td>
<td>52% (40% to 60%)</td>
<td>4</td>
<td>336</td>
</tr>
<tr>
<td>Gynaecological</td>
<td>60% (50% to 71%)</td>
<td>6</td>
<td>372</td>
</tr>
</tbody>
</table>

Traditional Management of Cancer Pain
Is there a role for functional radiosurgery?
• 1953: Luft and Olivecrona
  – Hypophysectomy to halt growth of hormonally sensitive tumors via pituitary de-stimulation
  – Patients also experiencing extreme bony met pain
  – Surprise side effect of the procedure was *complete relief of bone met pain*
History (continued)

• Others began performing sx hypophysectomy
  – Hardy et al (1971): transphenoidal ablation
  – Zervas et al (1972): RF coagulation

• Chemical hypophysectomy (EtOH injection into sella turcica)

• Direct electrical stimulation
Results

- In 1101 reported hypophysectomy, 64.4% of patients became pain free
  - Surgical: 70% of 334 cases
  - Chemical: 61.9% of 767 cases
Mechanism of pain relief associated with hypophysectomy

- Very poorly understood
- Postulated mechanisms
  - Alpha-endorphins?
  - Neurotransmissive properties of ADH?
  - Pituitary inhibition system?
- Seems unrelated to level of hormone production dysfunction
- More research needed
Gamma Knife Hypophysectomy

- Backlund et al (1972): first published gamma hypophysectomy
  - Rx = 25 krad max point (250Gy)
  - Only 8 patients, all breast cancer with painful bony metastasis
    - In patients surviving long enough for follow-up, “treatment obviously yielded relief of pain and an increased sense of well-being”

Sella turcica with the position of the sagittal (a) and frontal (I,) sections of the 90%, 50%, and 10% isodose lines when a single target is irradiated with a 3 x 5 beam (Backlund 1972)
• Nine patients with intractable bony metastasis pain
  – Variable histology (prostate, lung, et al)
• 160 Gy max (80Gy coverage of) to pituitary
  – Target center: border b/w gland & stalk
  – one 8mm or two 4mm shots
  – Principle avoidance structure is optic chiasm
    [dmax < 12Gy (ideally <8Gy)]
• All patients became pain free within a few days as long
  as they lived with no recurrence
• Authors eventually treated several more, all with similar
  results
Another Virtual Cone Application?
Epidemiology

- Affects approximately 2.2 million adults per year
- Estimated 12 month prevalence:
  - 1.2%
- Estimated lifetime prevalence:
  - 2.3%
- Roughly 1/3 fail to experience clinical benefit from CBT or SSRI
  - Of those, 2/3 fail to benefit from 2nd-line antipsychotic medication
- 3% to 5% of patients with OCD remain severely impaired & refractory to treatment

Yale-Brown Obsessive Compulsive Scale (Y-BOCS)

Description
The Yale-Brown Obsessive Compulsive Scale (Y-BOCS) is a 10-item scale designed to measure the severity and type of symptoms in people with obsessive-compulsive disorder (OCD) over the past seven days. The symptoms assessed are obsessions and compulsions. This scale is useful in tracking OCD symptoms at intake and during/after treatment.

Validity
This scale was validated by Goodman et al. (1989b) who found that the Y-BOCS was significantly correlated with two independent measures of OCD. The same study also showed that the Y-BOCS is sensitive to changes in OCD symptoms. The Y-BOCS also has high internal consistency and high interrater reliability (Goodman et al., 1989a).

Interpretation
Total Y-BOCS scores range from 0 to 40, with higher scores indicating greater severity of OCD symptoms. Scores on the obsession and compulsion subscales range from 0 to 20, but only the total Y-BOCS score is interpreted. Total scores can be split into five categories, based on severity of symptoms. People who have a total Y-BOCS score:

Under 7 are likely to be subclinical,
8-15 are likely to have a mild case of OCD,
16-23 are likely to have a moderate case of OCD,
24-31 are likely to have a severe case of OCD,
32-40 are likely to have an extreme case of OCD.

Developer
Treatment
Basis of Radiosurgery

- PET studies indicate abnormal regional metabolism b/w caudate, orbitofrontal cortex, and thalamus mitigated by therapy
- Resting-state fMRI studies consistently show increased orbitofrontal-striatal connectivity

Figure 1. Significant within-group striatal functional connectivity maps in control subjects and obsessive-compulsive disorder (OCD) patients. Results are displayed on an inflated viewing of the cortical surface of the Population Average Landmark and Surface-Based Atlas (62).
Basis of Radiosurgery (cont’d)

• Orbital and anterior cingular efferents traverse the anterior capsule in higher primates
• Recent diffusion imaging studies confirm concordant geography of the fibers in the human brain
Treatment of Resistant Obsessive-Compulsive Disorder With Ventral Capsular/Ventral Striatal Gamma Capsulotomy: A Pilot Prospective Study

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Benjamin D. Greenberg, M.D., Ph.D.
Georg Norén, M.D., Ph.D.
Miguel Montes Canteras, M.D., M.Sc.
Geraldo F. Busatto, M.D., Ph.D.
Maria Eugênia de Mathis, Psy.D.
Anita Taub, Psy.D., M.Sc.
Carina Chaubet D’Alcante, Psy.D.
Marcelo Queiroz Hoexter, M.D.
Fernando Sauerbronn Gouvea, M.D.
Janaina Philippi Cecconi, M.D.
André F. Gentil, M.D.
Ygor Arzeno Ferrão, M.D., M.Sc., Ph.D.
Daniel Fuentes, Psy.D., Ph.D.
Cláudio Campi de Castro, M.D., Ph.D.
Cláudia C. Leite, M.D., Ph.D.
João Victor Salvajoli, M.D., Ph.D.
Fábio L. S. Duran, M.D., Ph.D.
Steven Rasmussen, M.D.
Eurípedes Constantino Miguel, M.D., Ph.D.

A subgroup of obsessive-compulsive disorder (OCD) patients remains refractory to conventional treatments. For them, a new stereotactic radiosurgery has been recently developed: the ventral capsular/ventral striatal (VC/VS) gamma capsulotomy. The authors aim to report efficacy and adverse events of VC/VS gamma capsulotomy. Five refractory OCD patients were selected. The authors assessed OCD, anxiety and depressive symptoms, and side effects pre- and postoperatively. Three patients (60%) met response criteria 48 months after surgery. Adverse effects were episodic and transient. Ventral capsular/ventral striatal gamma capsulotomy holds therapeutic promise, with few adverse effects.


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http://neuropsychiatryonline.org

T1-Weighted Axial and Coronal MRI Slices With Para-Magnetic Contrast (Gadolinium) Depicting Postoperative Ventral Capsular/Ventral Striatal Gamma Capsulotomy Lesions in Patients A and E.
T2-Weighted Coronal MRI Slices Depicting Postoperative Ventral Capsular/Ventral Striatal Gamma Capsulotomy Lesions in 5 Patients

Yale-Brown Obsessive Compulsive Scale (Y-BOCS) Scores Over 48 Months of Follow-Up for Five Patients Who Underwent Ventral Capsular/Ventral Striatal Gamma Capsulotomy
Radiosurgical Capsulotomy

Historically done on a Gamma Knife

- Prescription
  - 140Gy to 200Gy dmax to bilateral anterior interior capsule

- Downsides
  - Slow treatment (~5h)
  - Traditionally requires stereotactic frame placement
Reports and Results on Gamma Knife Bilateral Radiosurgical Capsulotomies for OCD

<table>
<thead>
<tr>
<th>Author</th>
<th>Patient No.</th>
<th>Preoperative YBOCS</th>
<th>Last YBOCS</th>
<th>Follow-up, mo</th>
<th>Radiation Dose, Gy</th>
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<tr>
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³OCD, obsessive compulsive disorder; YBOCS, Yale-Brown Obsessive Compulsive Scale.
• Largest series to date, 55 patients (40 avail for long term f/u)
• By 3y, 75% of patients had >35% reduction in symptoms
• 1/55 Grade 5 toxicity from radionecrosis
Other Under-treated Functional SRS Indications

- Dystonia (120Gy to STN)
- Thalamic pain (130Gy to VPN)
- Obsessive compulsive disorder (180Gy to AC)
- Epilepsy
  - hypothalamic hamartomas (~15Gy to hamartoma)
  - mesial temporal sclerosis (40-48Gy to amygdala)
- Sphenopalatine neuralgia (80Gy to SPG)
- Chronic cluster headaches (80Gy to SPG or TGN)
Conclusions

High-quality MLC-based (Virtual Cone) functional SRS is now feasible on the Edge™ platform:
- plan template can replicate 4-mm GK helmet dosimetry
- template can be re-optimized to mimic other helmet dosimetrys
- doesn’t require patient specific QA
- fits into normal clinical workflow

Conservatively, across just US market, multiple millions of potential indications

Barriers
- 1) Awareness by providers
- 2) Deployment of technology
- 3) Native conservativeness of US radiation oncologists for non-oncologic indications
- 4) Slow transition of neurosurgeons into comfort on non-GK platform


2012 - Brontë-Stewart - Deep brain stimulation - Neurol Clin Pract

2004 - Okun - Development and initial validation of a screening tool for PD surgical candidates - Neurology