Functional Neurosurgical Applications of Modern Precision Radiosurgery

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THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

Knowledge that will change your world

Disclosures

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

Function

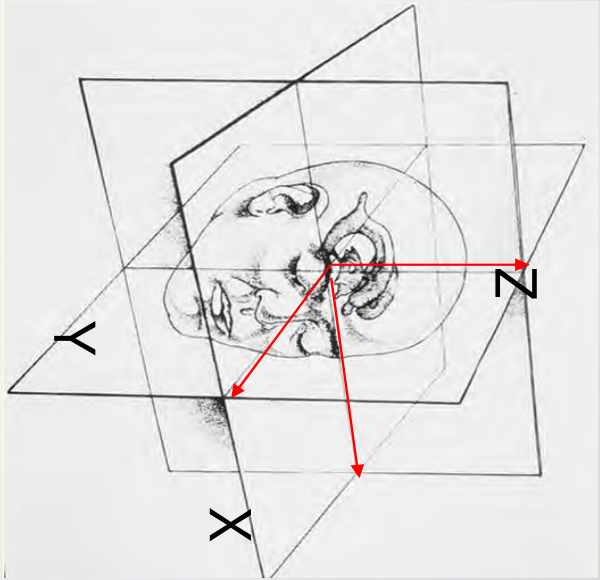
- Neurosurgical inte
when physiology is
but anatomy may
be normal
- Historically, require
ablation or directio
of injurious chemic
phenol or ethanol)
- Developed in para
practice of stereota

First stereotaxic apparatus by Horsley, 1908 (not used in humans)

- Horsley 1
noch nicht b
- Spigel un
Routinemäs
Menschen, V
- Traugott
Erstmalige G
Thalamuske

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.*
- 2004 – First non-trigem LINAC fxnl SRS, *Frighetto*, *De Salles, 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

JNS

CLINICAL ARTICLE

J Neurosurg (Suppl 1) 125:160–165, 2016

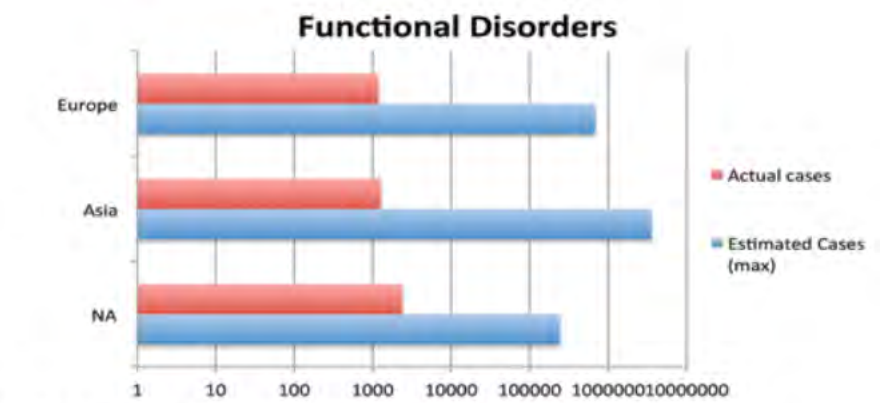
Worldwide variance in the potential utilization of Gamma Knife radiosurgery

Travis Hamilton, BS,[1] and L. Dade Lunsford, MD[2]

[1]Michigan State University College of Human Medicine, Lansing, Michigan; and [2]Department of Neurological Surgery, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania

Functional Radiosurgery

Under Utilized



Skull/Functional Disorder	NA	Asia	Europe
Incidence (per million)	120-2000	2000	2000
% Suitable for GKRS	23	44	46
Estimated Cases (max)	243340	3542880	683560
Actual cases	2372	1253	1178
% Utilization	0.97%	0.04%	0.17%

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.

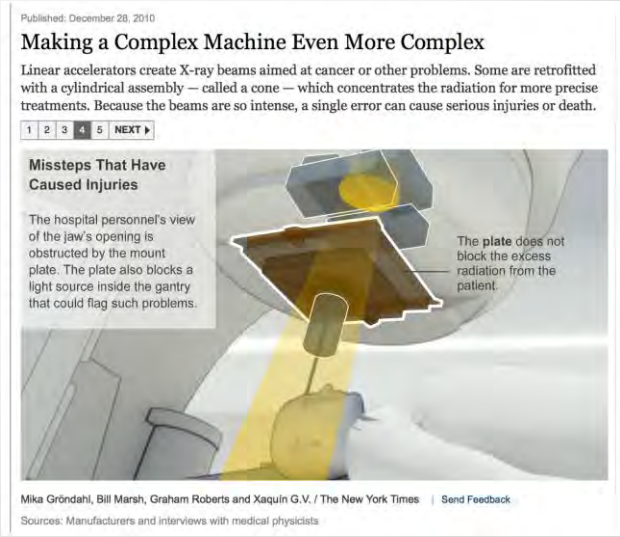
Hamilton, Travis, and L. Dade Lunsford. "Worldwide variance in the potential utilization of Gamma Knife radiosurgery." Journal of neurosurgery 125.Supplement 1 (2016): 160-165.

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, Toulose, etc



Published: December 28, 2010

Making a Complex Machine Even More Complex

Linear accelerators create X-ray beams aimed at cancer or other problems. Some are retrofitted with a cylindrical assembly — called a cone — which concentrates the radiation for more precise treatments. Because the beams are so intense, a single error can cause serious injuries or death.

1 2 3 4 5 NEXT

Missteps That Have Caused Injuries

The hospital personnel's view of the jaw's opening is obstructed by the mount plate. The plate also blocks a light source inside the gantry that could flag such problems.

The plate does not block the excess radiation from the patient.

Mika Gröndahl, Bill Marsh, Graham Roberts and Xaquin G.V. / The New York Times | Send Feedback

Sources: Manufacturers and interviews with medical physicists

For those with LINACs, is there a better way?

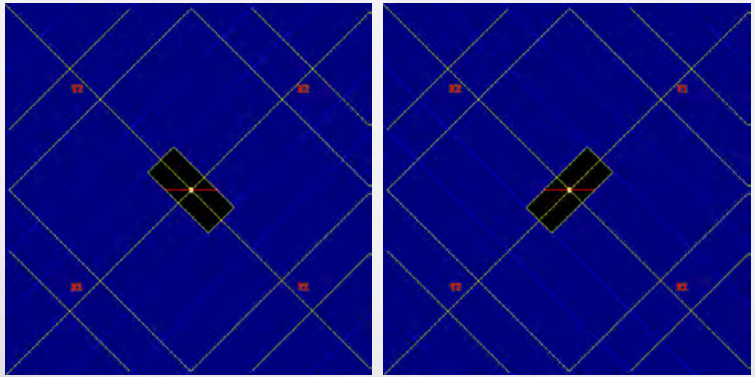
- Robust targeting
- Reliable treatment delivery
- Maximal patient convenience and comfort
  - completely non-invasive (frameless)
  - expedited treatment time

Virtual Cone (VC) on the Edge™

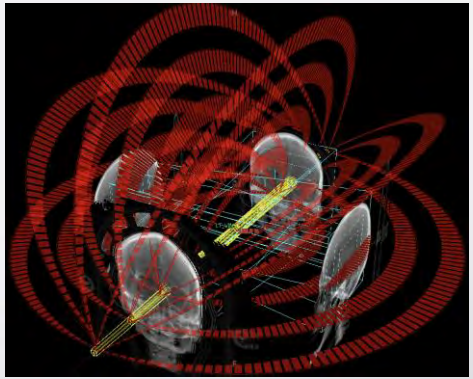
- MLC-based (Virtual Cone) VMAT SRS developed by Dr. Richard Popple (UAB) in concert with VMS
  - Pre-calculated fixed modulation pattern VMAT plan, with static MLC leaves
- Pre-defined MLC control point sequence designed to create a 4 mm to 5 mm diameter dose distribution
- Model using standard dose 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 α sin(gantry angle)

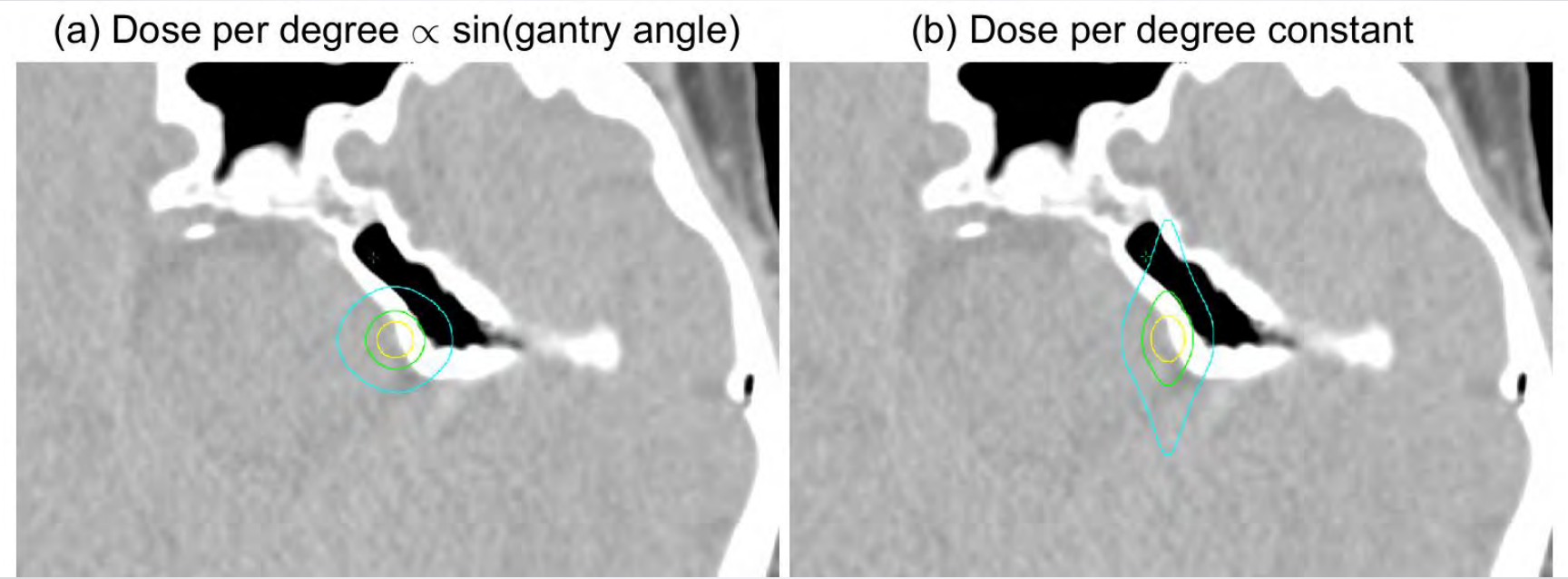


MLC aperture



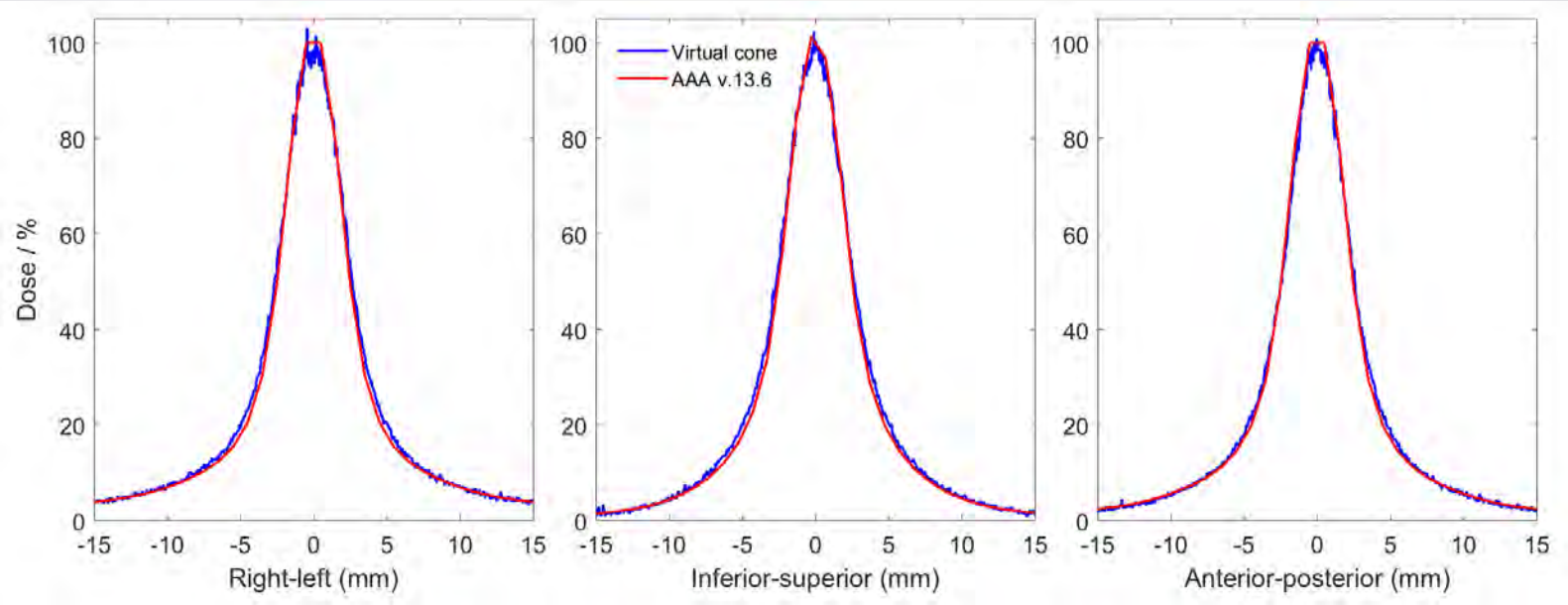
Arc geometry

Comparison of Dose Profiles in Virtual Cone Using Dose ∝ sin (gantry) vs constant dose



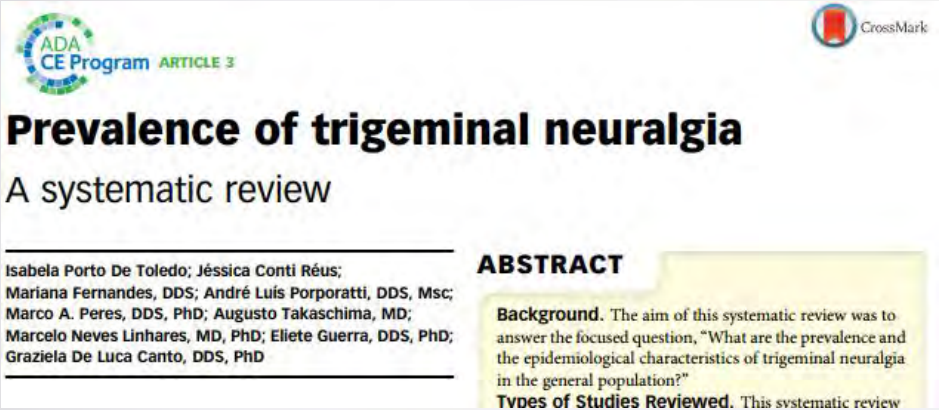
Dose distribution for a virtual cone treatment plan having dose per degree a) proportional to sine of the gantry angle and b) constant. Displayed isodose lines correspond to 50% (yellow), 25% (green), and 10% (cyan) of the maximum dose.

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



ADA CE Program ARTICLE 3

CrossMark

Prevalence of trigeminal neuralgia

A systematic review

Isabela Porto De Toledo; Jéssica Conti Réus; Mariana Fernandes, DDS; André Luís Porporatti, DDS, Msc; Marco A. Peres, DDS, PhD; Augusto Takaschima, MD; Marcelo Neves Linhares, MD, PhD; Eliete Guerra, DDS, PhD; Graziela De Luca Canto, DDS, PhD

ABSTRACT

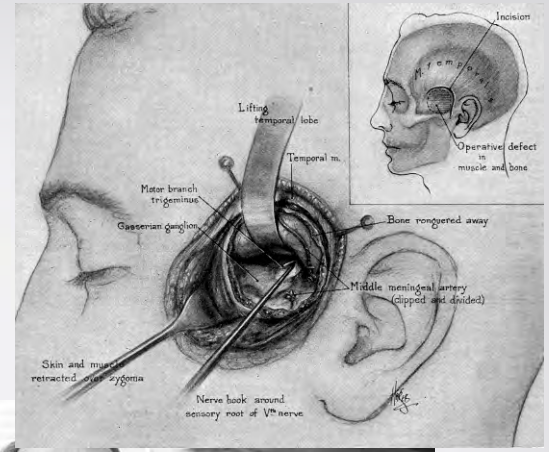
Background. The aim of this systematic review was to answer the focused question, "What are the prevalence and the epidemiological characteristics of trigeminal neuralgia in the general population?"

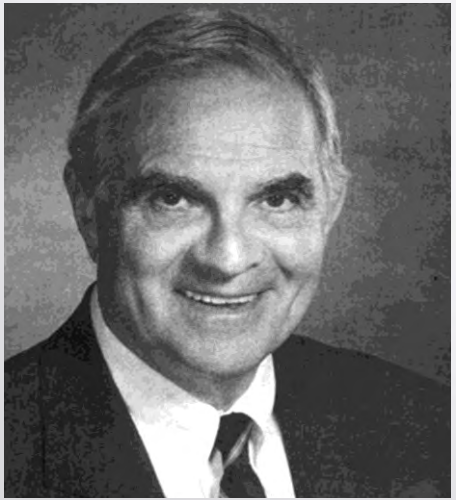
Types of Studies Reviewed. This systematic review

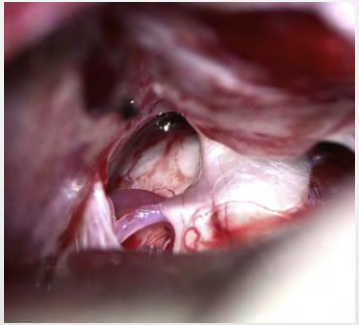
- Increasingly recognized as more common than previously thought
- Revised estimates of prevalence are 0.03 – 0.3%
  - Conservatively 90000 in the United States
  - Previously estimated at ~40000

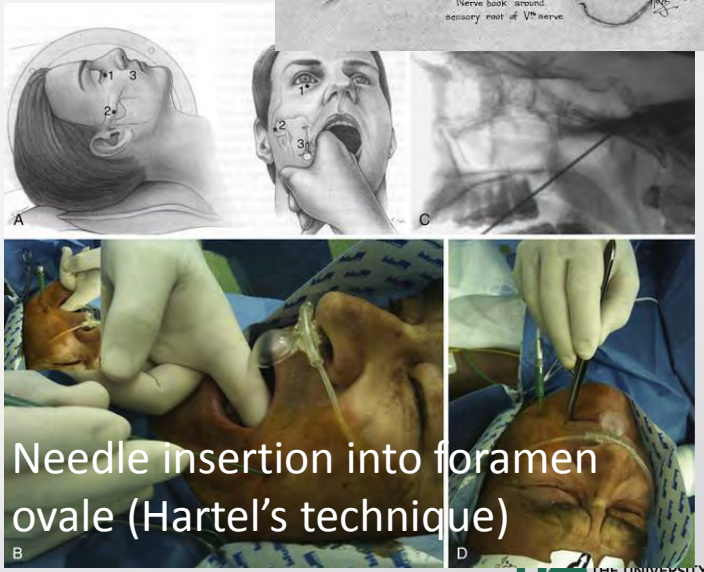
Trigeminal Neuralgia (cont'd)

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









Needle insertion into foramen ovale (Hartel's technique)

Trigeminal Neuralgia SRS Studies

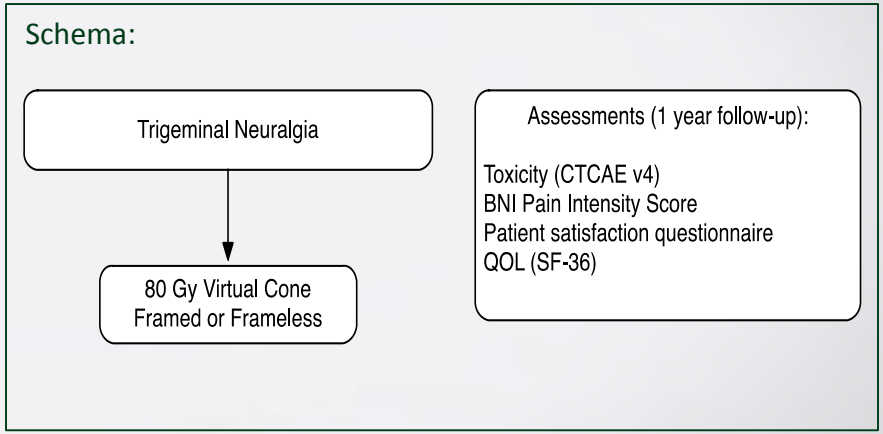
Table 3 Selected studies using various SRS modalities and respective pain control and complication rates

Modality	Publication	No. of patients	Dose (Gy)	Median follow-up (mo)	Pain control	Complications
Gamma Knife	Maesawa et al[3] (2001)	220	80 (48.6%); range, 60-90	24.0	Pain relief at 1 y: 70.3%	Ipsilateral facial numbness: 10.2%
	Kondziolka et al[7] (2010)	503	80 (88%); range, 60-90	24.0	BNI I-III at 1 y: 80%; recurrence rate: 42.9%	Ipsilateral facial paresthesias: 10.5%
	Lee et al (2015)[23]	133	80 (all)	22.8	Recurrence rate: 31%	Ipsilateral facial numbness: 10%
CyberKnife	Adler et al[5] (2009)	46	73.5 (mean maximal)	14.7	Excellent or good patient-reported outcome: 72%/24%	Ipsilateral facial numbness: 15%
	Tang et al (2011)[24]	14	80.5 (mean maximal)	20.4	Initial response: 92.8%	Ipsilateral facial numbness: 14.2%
	Lazzara et al (2013)[25]	17	73.06 (mean)	5.0 (mean)	Initial partial or complete response: 86%	Dysesthesia or numbness: 11.8%
	Karam et al[21] (2014)	25	64 (mean)	28.0	Freedom from severe pain (BNI IV-V): 72%	New facial numbness or pain: 28%
LINAC-based with flattening filter	Goss et al[12] (2003)	25	90	12.0	Excellent or good pain relief: 76%/24%	Ipsilateral facial numbness: 32%
	Richards et al[11] (2005)	28	80	12.0	Complete or significant pain relief: 75%	Ipsilateral facial numbness: 10.7%
	Smith et al[14] (2011)	169	90 (83.4%), range, 70-90	28.8	Excellent or good pain relief: 88.5%	Any degree of numbness: 49.7%
LINAC-based, FFF	Current study	36	75 (median)	5.5 (mean)	Pain relief by first follow-up: 88.5%; medication-free pain relief: 15%	New dysesthesia or hypoesthesia: 0%

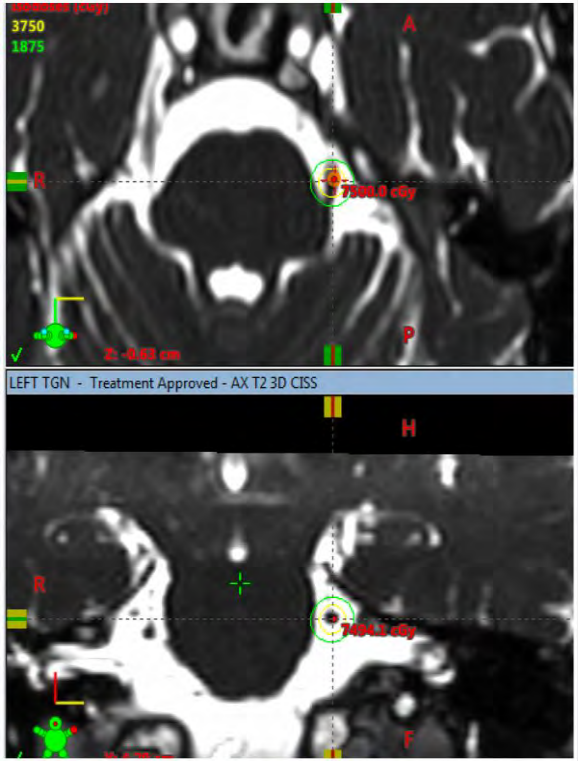
BNI, Barrow Neurological Institute pain score; CK, CyberKnife; FFF, flattening filter free; GK, Gamma Knife; LINAC, linear accelerator.

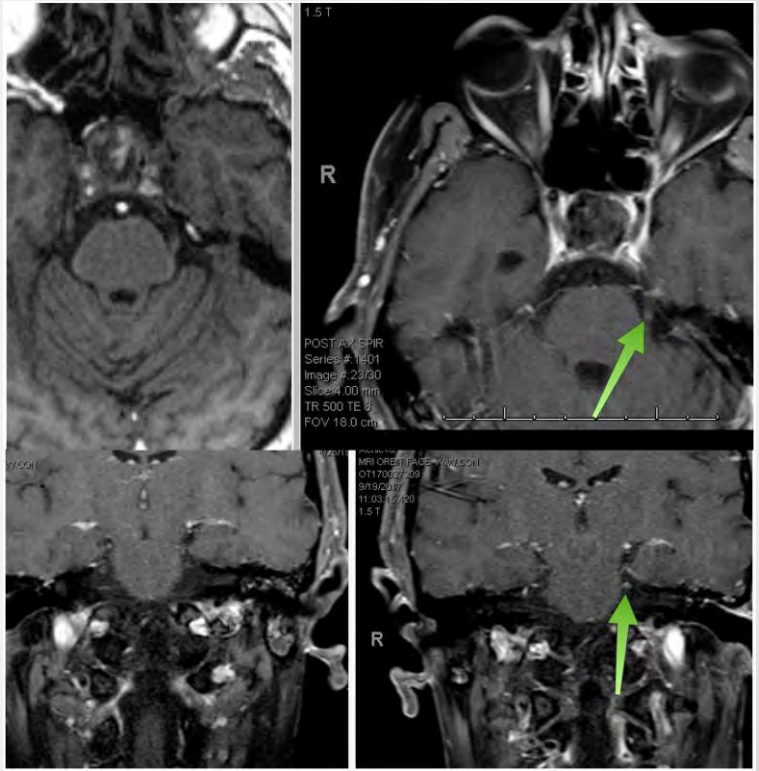
UAB Virtual Cone SRS for Trigeminal Neuralgia Trial (RAD 1501)

- **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).



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 accruement greatly increased with neurosurgeon engagement
- Plans to extend single-institutional phase of trial for additional accruement
- Search for multi-institutional partner narrowed to one of a few candidate institutions

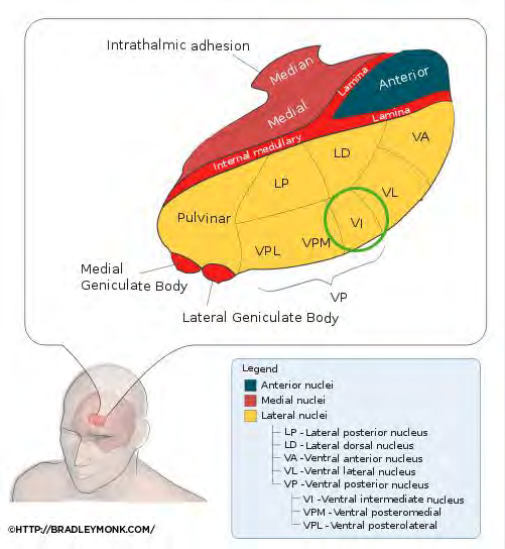
- Results:
  - Pain relief consistent with previous literature reported rate
  - No unusual or unexpected toxicity
  - Patients pleased with ease and comfort of procedure

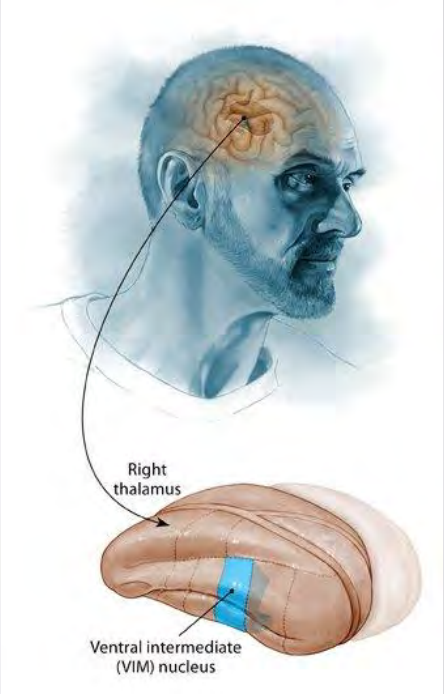
Essential & Parkinsonian Tremor

- 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

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Paul Krack, MD, PhD
Alexandre Eusebio, MD, PhD
Marianne Vaugoyeau, PhD
Marwan Hariz, MD, PhD
Jean Philippe Azulay, MD, PhD
Jean Régis, MD

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ABSTRACT

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

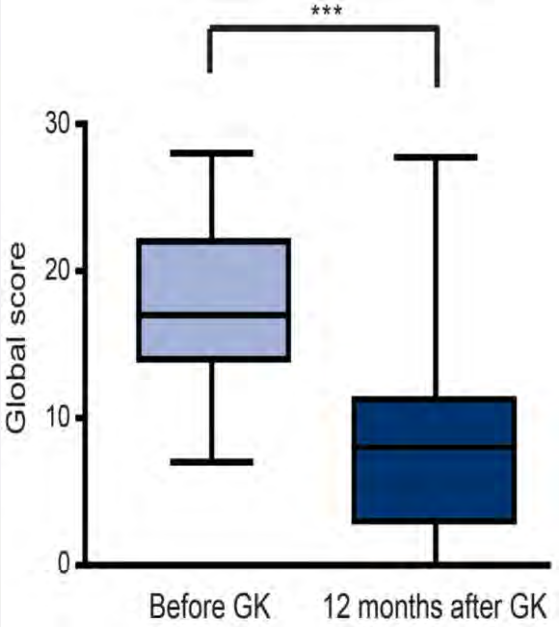
Methods: Fifty patients (mean age: 74.5 years; 32 men) with severe refractory tremor (36 essential, 14 parkinsonian) were treated with unilateral GKT. Targeting of the ventral intermediate nucleus (Vim) was achieved with Leksell Gamma Knife with a single shot through a 4-mm collimator helmet. The prescription dose was 130 Gy. Neurologic and 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.

Neurology® 2015;85:1562–1568



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

UAB RAD 1601 Structure

SCHEMA

s trial will initially target enrollment of twenty patients at a single institution to confirm that all dy procedures and assessments are feasible and safe.

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

Characterize
- Assess baseline tremor/ADL score
- Acquire baseline imaging

Treat
- 130Gy Virtual Cone radiosurgical thalamotomy

Follow
- Clinical neurology: tremor/ADL assessment 3, 6, 12 mo
- MRI: immediately pre-tx, 2wks, 6 mo, 12 mo

6.2.2 Schedule of Imaging*

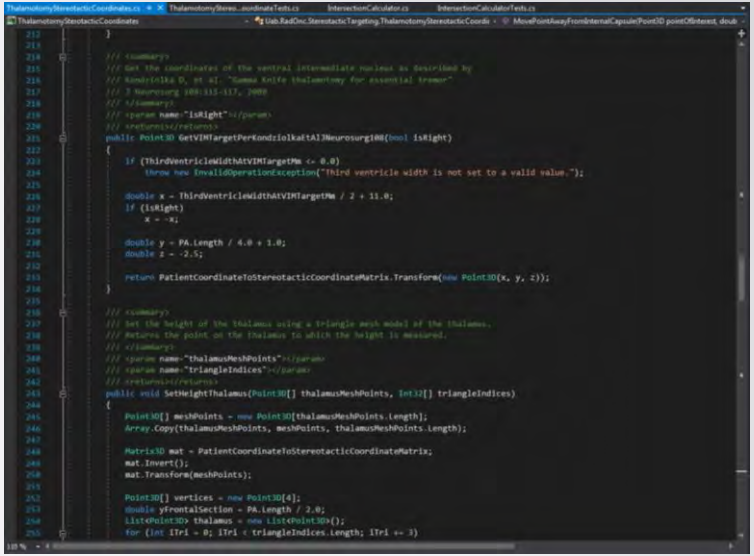
Image Sequence	Pre-RS	2 weeks	6 months	12 months
T1 weighted image	X	X	X	X
T2 weighted image	X	X	X	X
Diffusion Weighted Image	X		X	X
Resting fMRI	X	X	X	X
Task Based fMRI	X		X	X
3T Novel Targeting Study (UAB)	X			
7T Novel Targeting Study (Auburn University)	X			

PATIENT SELECTION CRITERIA

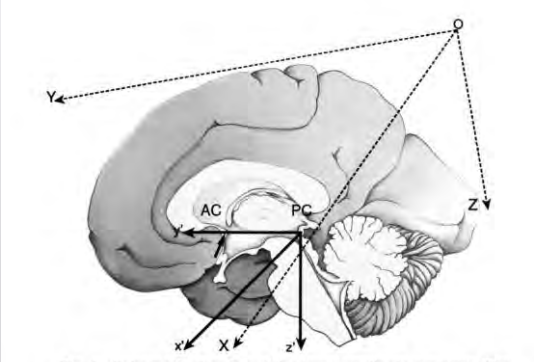
4.1 Inclusion Criteria

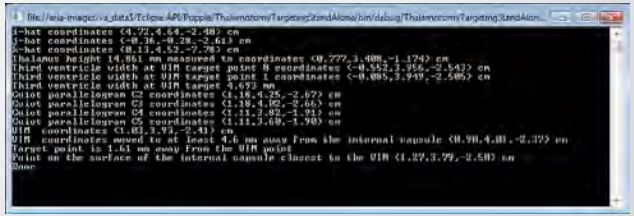
Automated stereotactic targeting

- 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 Dmax (65 Gy to 4.5-mm VC)
- 20% (26Gy) IDL line kept medial to IC



```
        }

        /// <summary>
        /// Get the coordinates of the central intermediate nucleus as described by
        /// Kondziolka D, et al. "Gamma Knife thalamotomy for essential tremor"
        /// J Neurosurg 100:113-117, 2003
        /// </summary>
        /// <param name="isRight"></param>
        /// <returns></returns>
        public Point3D GetVIMTargetPerKondziolkaEtAlNeurosurg100(bool isRight)
        {
            if (ThirdVentricleWidthAtVIMTargetMm <= 0.0)
                throw new InvalidOperationException("Third ventricle width is not set to a valid value.");

            double x = ThirdVentricleWidthAtVIMTargetMm / 2 + 11.0;
            if (isRight)
                x = -x;

            double y = PA.Length / 4.0 + 1.0;
            double z = -2.5;

            return PatientCoordinateToStereotacticCoordinateMatrix.Transform(new Point3D(x, y, z));
        }

        /// <summary>
        /// Set the height of the thalamus using a triangle mesh model of the thalamus.
        /// Returns the point on the thalamus to which the height is measured.
        /// </summary>
        /// <param name="thalamusMeshPoints"></param>
        /// <param name="triangleIndices"></param>
        /// <returns></returns>
        public void SetHeightThalamus(Point3D[] thalamusMeshPoints, Int32[] triangleIndices)
        {
            Point3D[] meshPoints = new Point3D[thalamusMeshPoints.Length];
            Array.Copy(thalamusMeshPoints, meshPoints, thalamusMeshPoints.Length);

            Matrix3D mat = PatientCoordinateToStereotacticCoordinateMatrix;
            mat.Invert();
            mat.Transform(meshPoints);

            Point3D[] vertices = new Point3D[4];
            double yFrontalSection = PA.Length / 2.0;
            List<Point3D> thalamus = new List<Point3D>();
            for (int iTri = 0; iTri < triangleIndices.Length; iTri += 3)
```

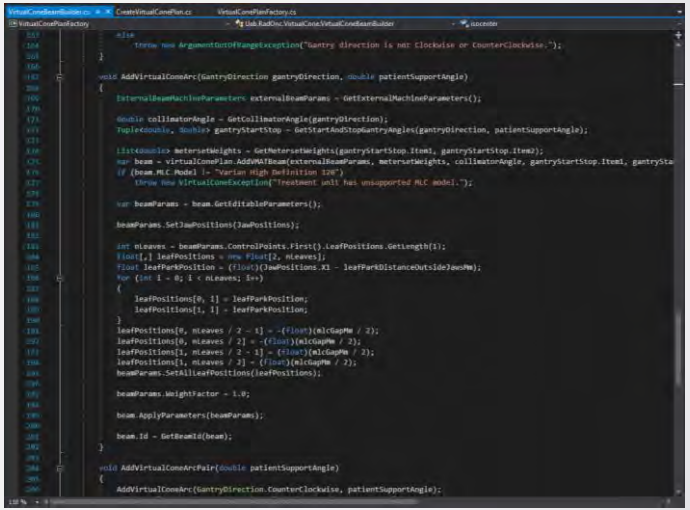




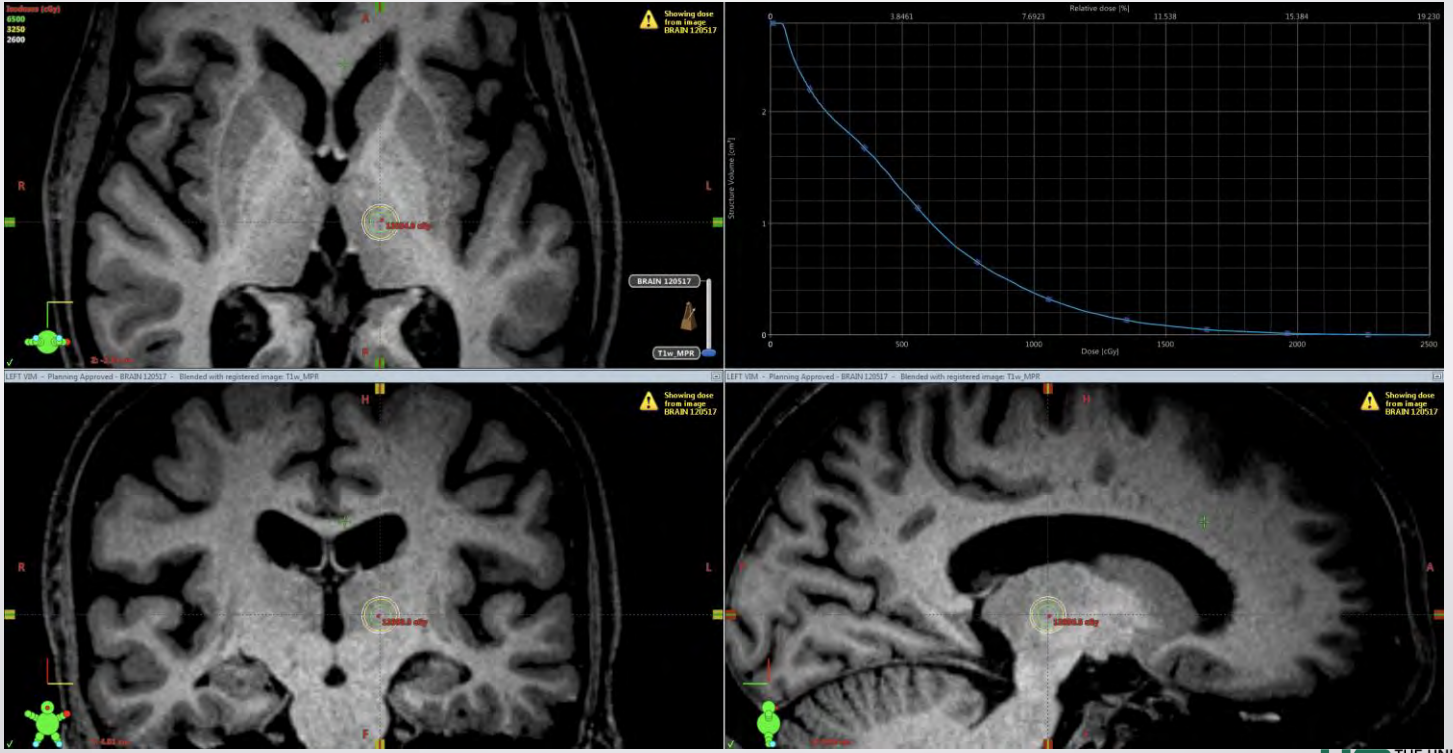
```
i-hat coordinates <4.72,4.64,-2.48> cm
j-hat coordinates <-0.06,-0.28,-2.61> cm
k-hat coordinates <8.13,4.52,-7.78> cm
Thalamus height 14.861 mm measured to coordinates <0.277,3.408,-1.174> cm
Third ventricle width at VIM target point A coordinates <-0.552,3.956,-2.543> cm
Third ventricle width at VIM target point I coordinates <-0.085,3.949,-2.585> cm
Third ventricle width at VIM target 4.672 mm
Quiet parallelogram C2 coordinates <1.16,4.25,-2.67> cm
Quiet parallelogram C3 coordinates <1.38,4.05,-2.66> cm
Quiet parallelogram C4 coordinates <1.11,3.82,-1.91> cm
Quiet parallelogram C5 coordinates <1.11,3.60,-1.90> cm
VIM  coordinates <1.83,3.93,-2.41> cm
VIM  coordinates moved to at least 4.6 mm away from the internal capsule <0.98,4.01,-2.37> cm
Target point is 1.61 mm away from the VIM point
Point on the surface of the internal capsule closest to the VIM <1.87,3.99,-2.50> cm
Done
```

Scripted treatment planning

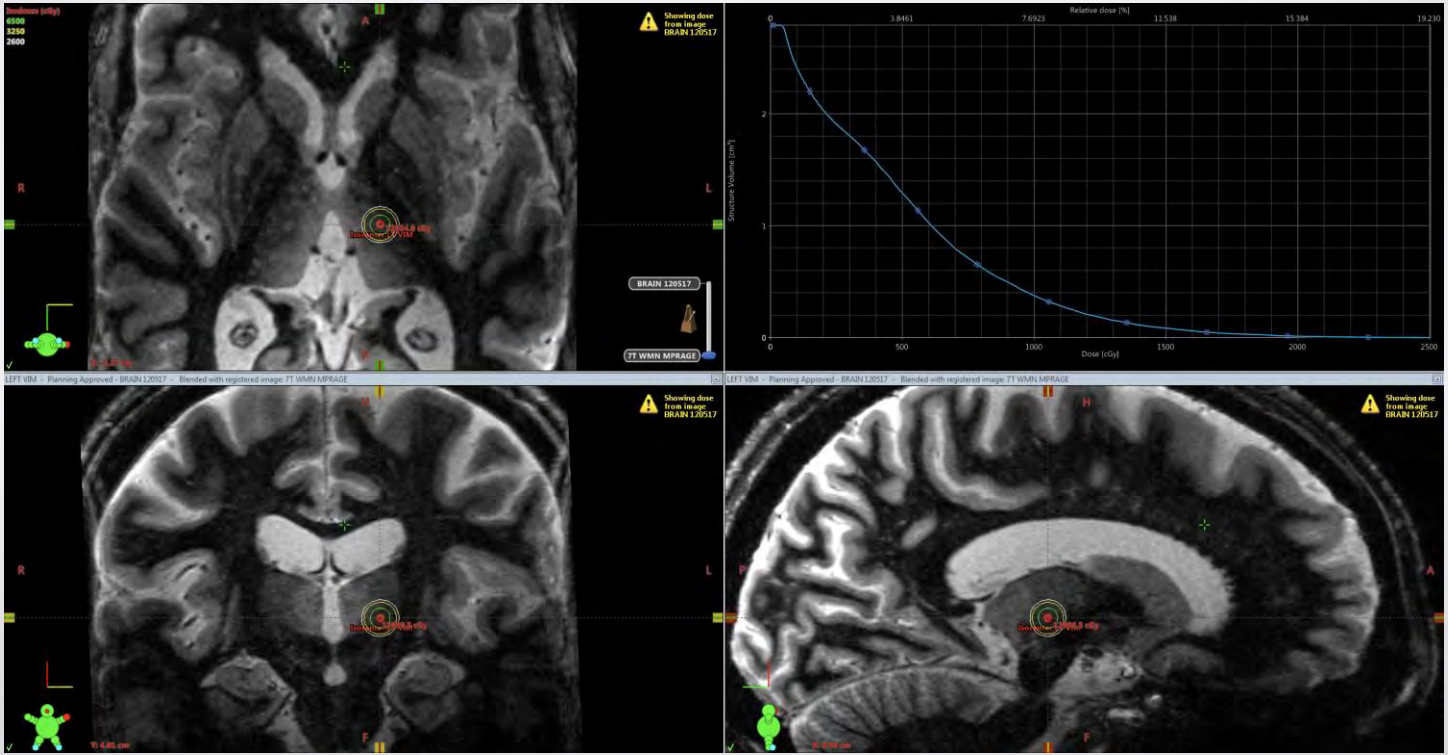
- 0.8 mm grid size
- 10 framework agent servers
- Calculation time
  - AAA 13.6 - 23.4 min
  - Acuros XB 13.6 (plan dose) – 14.8 min
  - Acuros XB 13.6 (field by field) – 2.8 min
- Soon: GPU acceleration for massively parallel computation



SRS thalamotomy plan (MPRAGE)

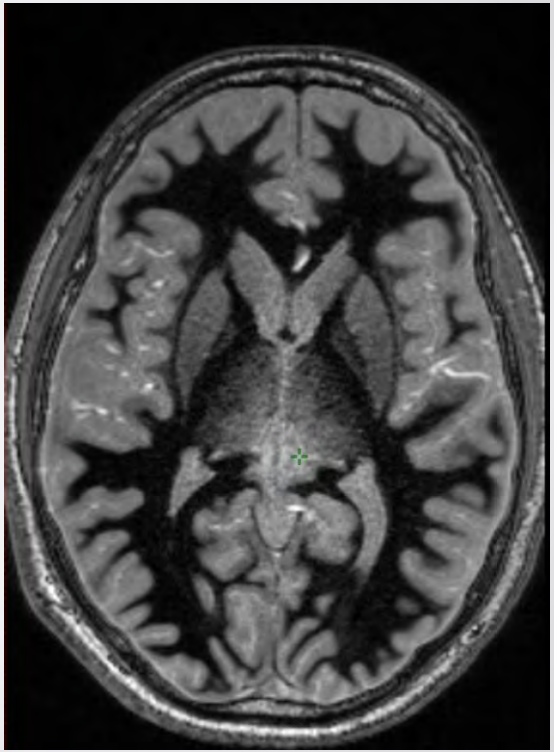


SRS thalamotomy plan (FGATIR)

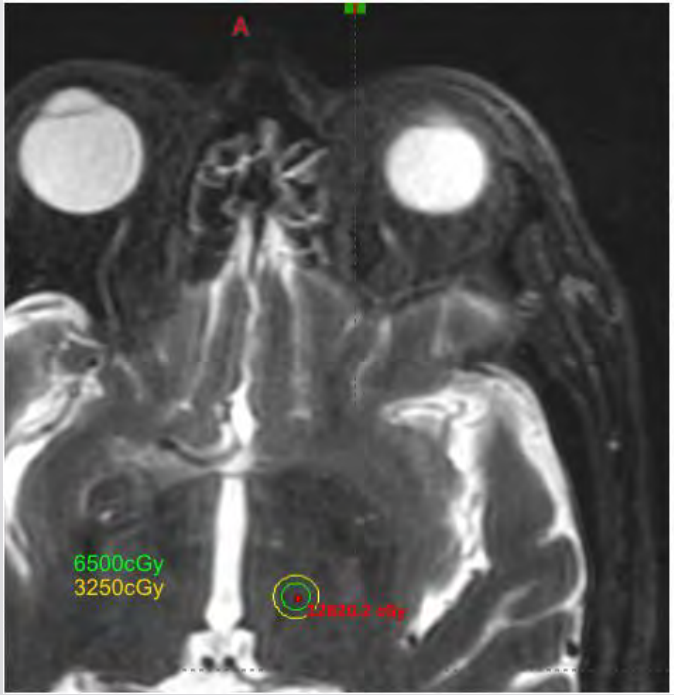


FGATIR sequence on 3T and 7T

- 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

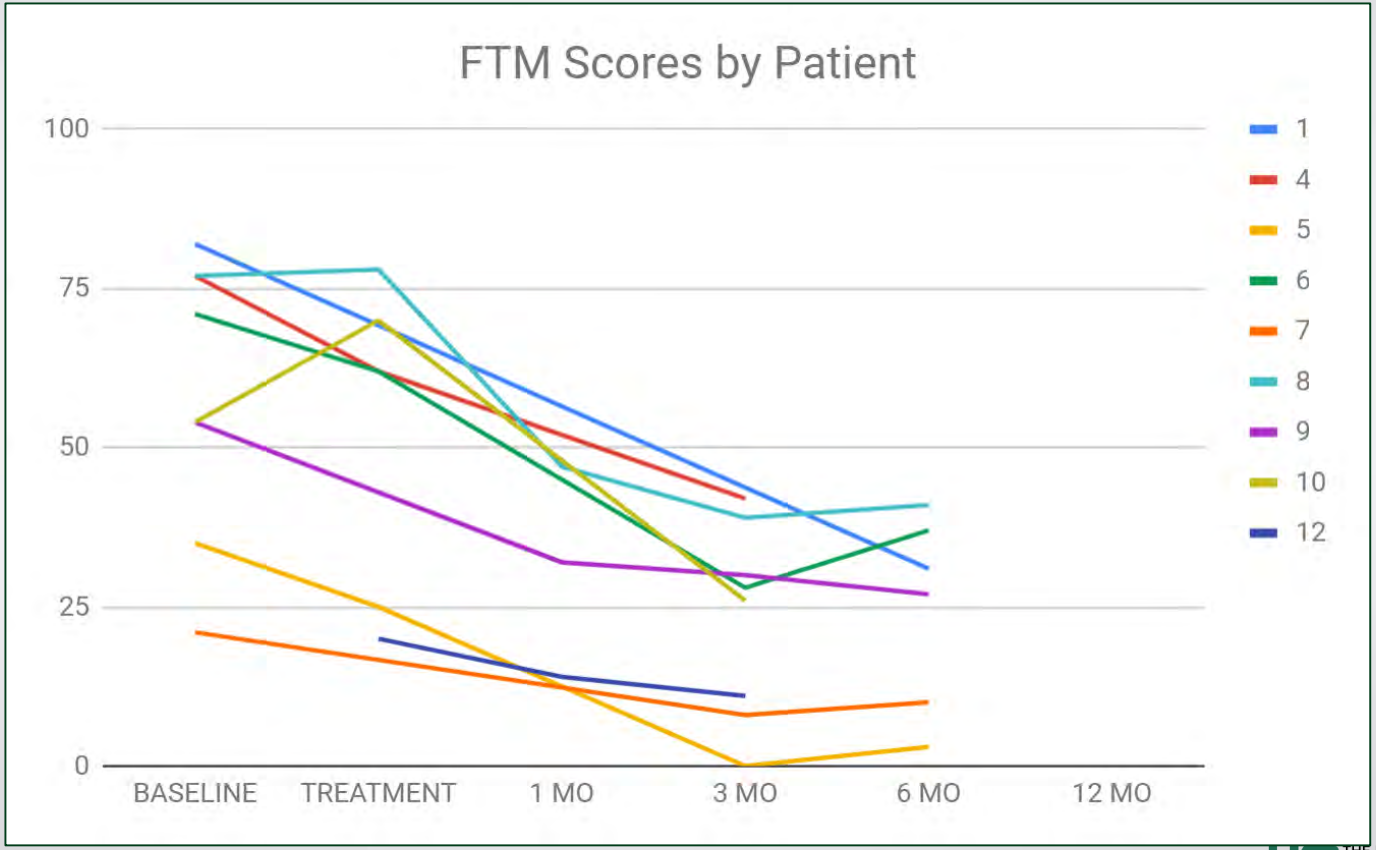


In vivo dose delivery verification!

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

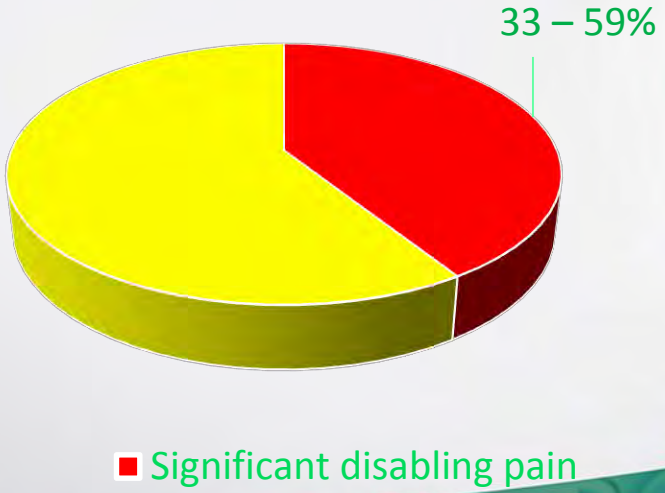


Other potential applications we are exploring:

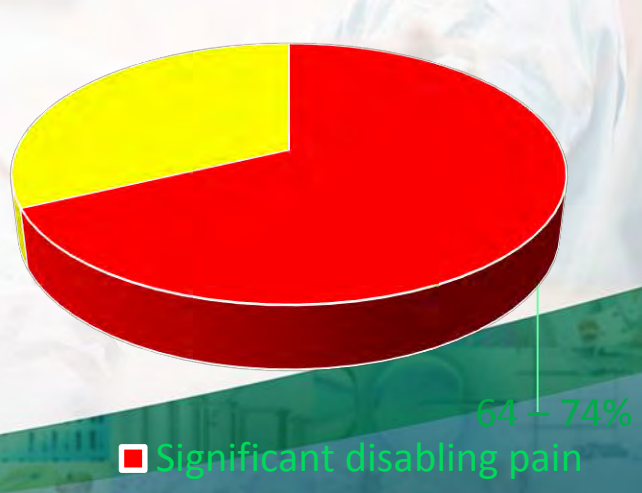
Radiosurgical Management of Intractable Pain in Terminal Cancer Patients

Pain in cancer patients

Patients undergoing cancer treatment



Patients with advanced disease



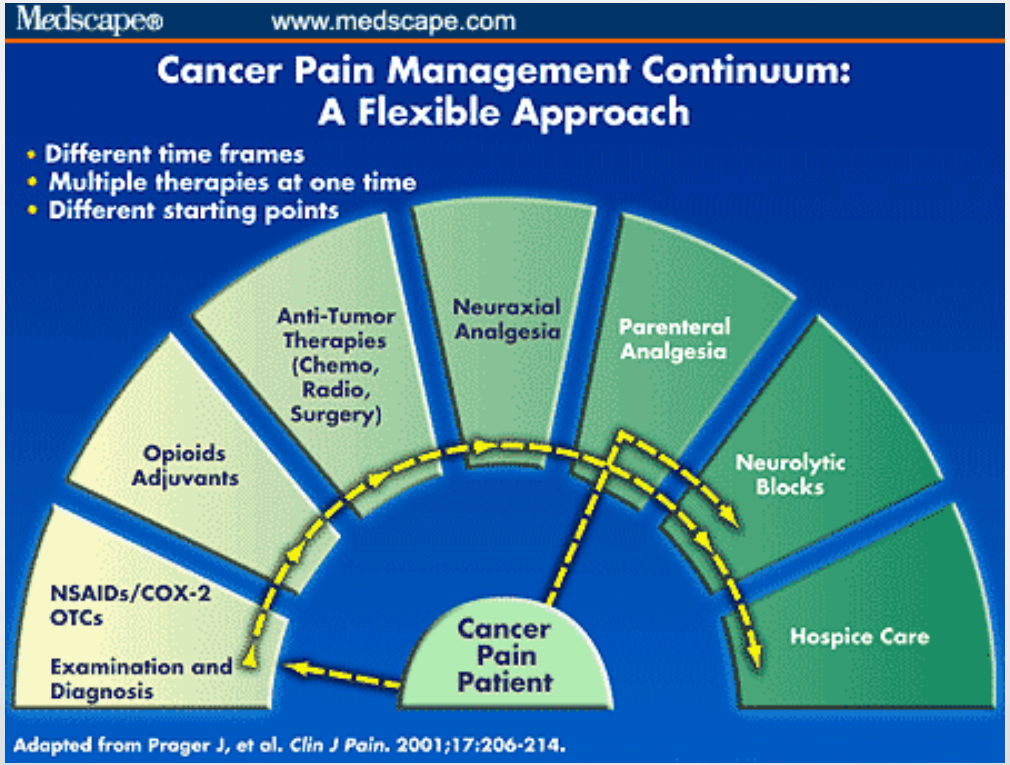
Van den Beuken-van Everdingen, M. H. J., et al. "Prevalence of pain in patients with cancer: a systematic review of the past 40 years." *Annals of oncology* 18.9 (2007): 1437-1449.

Prevalence of pain among different types of cancer

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

Van den Beuken-van Everdingen, M. H. J., et al. "Prevalence of pain in patients with cancer: a systematic review of the past 40 years." *Annals of oncology* 18.9 (2007): 1437-1449.

Traditional Management of Cancer Pain



Is there a role for functional radiosurgery?

History of Functional Neurosurgery for Cancer Pain

- 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*

EXPERIENCES WITH HYPOPHYSECTOMY IN MAN*

ROLF LUFT, M.D., AND HERBERT OLIVECRONA, M.D.
Division of Endocrinology, Department of Internal Medicine, and Department of Neurosurgery, Serafimerlasarettet, Stockholm, Sweden

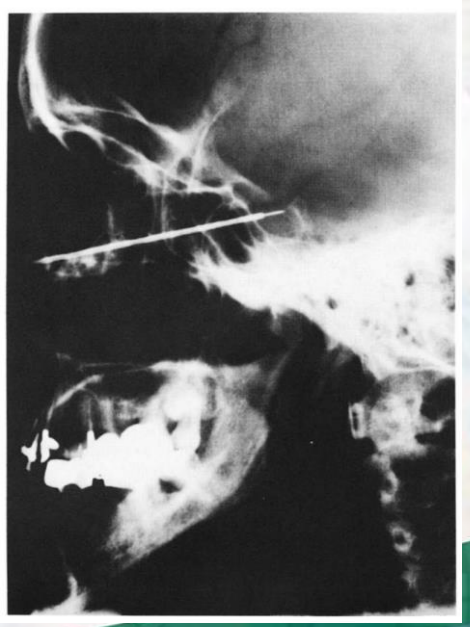
(Received for publication January 13, 1953)

THE present investigation concerns the effect of removal of the pituitary gland in some conditions in which it was thought probable that hypophysectomy might favorably influence the future course of the primary disease.

From a clinical point of view there are three important questions connected with hypophysectomy in man: the rationale of the operation, our possibilities of judging of the completeness of the operation, and the pre- and postoperative treatment of the patient. These points will be discussed briefly, and a more detailed report will be given of the surgical procedure.

History (continued)

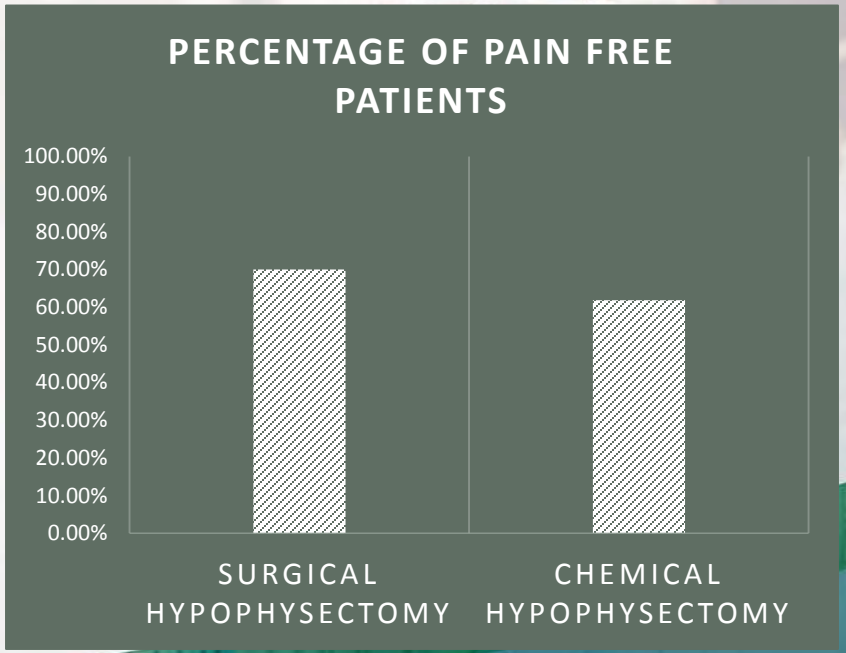
- Others began performing sx hypophysectomy
  - Forest et al (1959): I-131 implants
  - Hardy et al (1971): transphenoidal ablation
  - Zervas et al (1972): RF coagulation
- Chemical hypophysectomy (EtOH injection into sella turcica)
  - Greco et al (1959), Moricca (1974), Lipton et al (1978), Katz and Levin (1977)
- Direct electrical stimulation
  - Yanagida et al (1983)



Lateral view of stimulating electrode in a 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

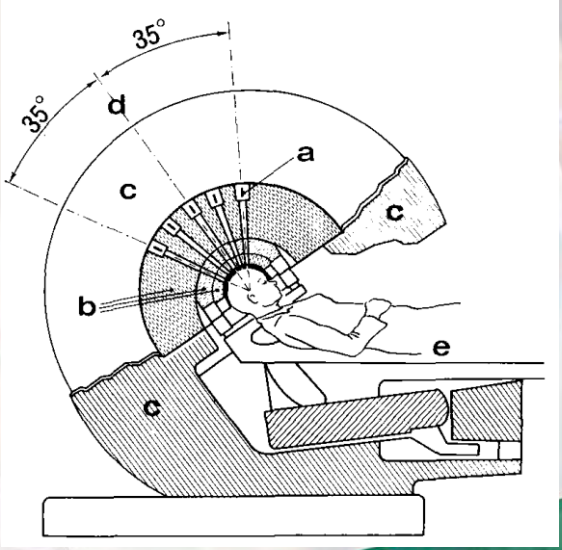


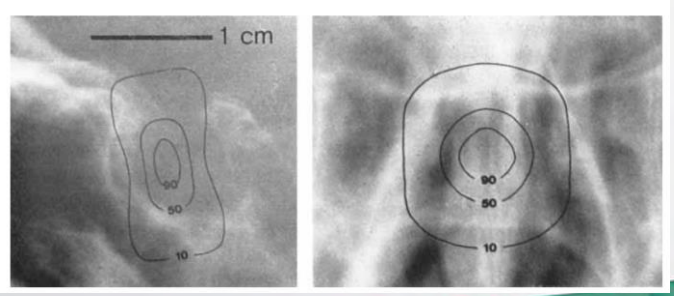
Mechanism of pain relief associated with hypophysectomy

- 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 “





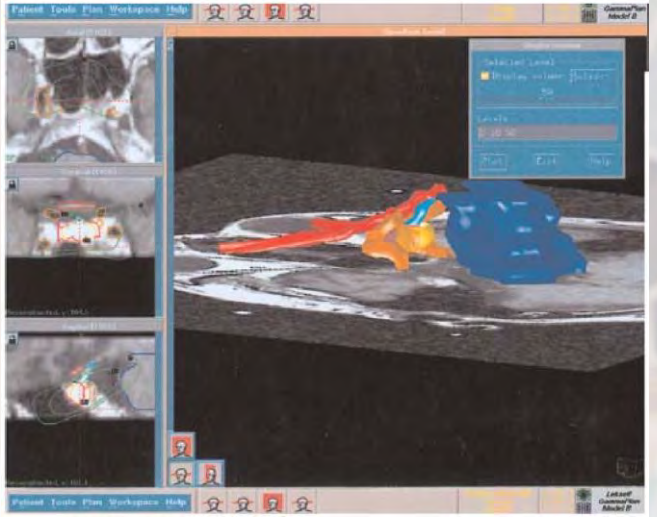
Sella turcica with the position of the sagittal [a) and frontal (I,) sections of the 90%, 50%, and 10% isodose lines when a single target is irradiated with a 3 x 5 beam (Backlund 1972)

GK Hypophysectomy (cont'd)

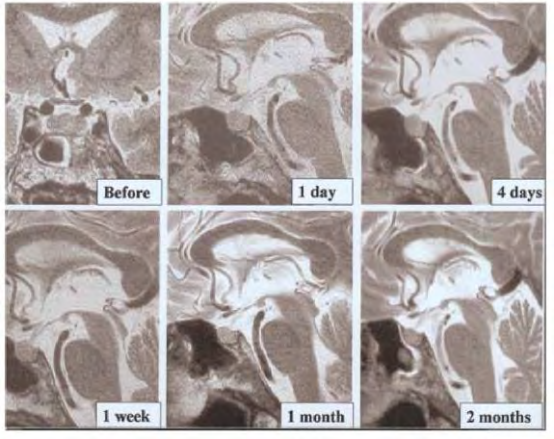
Gamma knife surgery for cancer pain–pituitary gland–stalk ablation: a multicenter prospective protocol since 2002

Motohiro Hayashi, M.D., D.M.Sc., Takaomi Taira, M.D., Ph.D., Mikhail Chernov, M.D., Seiji Fukuoka, M.D., Roman Liscak, M.D., Chung Ping Yu, M.D., Robert T. K. Ho, M.D., Jean Regis, M.D., Yoko Katayama, M.D., Ph.D., Yoriko Kawakami, M.D., Ph.D., and Tomokatsu Hori, M.D.

- 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



Target and the anatomical relationship between the target and the optics, carotid artery, pituitary gland, stalk, and brainstem.



Pre-GKS and post-GKS MR imaging changes, with radiation targeted to the pituitary gland stalk. Follow-up MR imaging within 2 months after GKS revealed no morphological changes.

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

Bloch, Michael H., et al. "Effects of ketamine in treatment-refractory obsessive-compulsive disorder." *Biological psychiatry* 72.11 (2012): 964-970.

Severity/Grading

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.

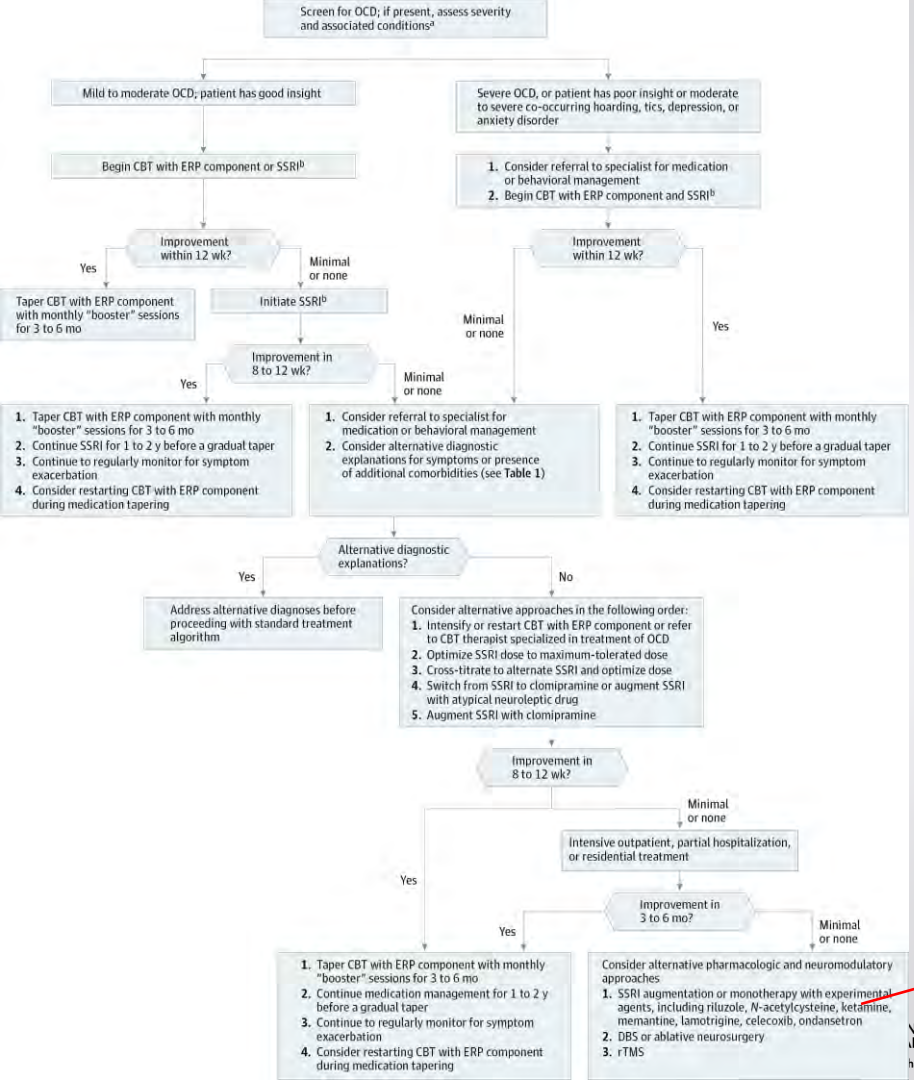
Validity
This scale was validated by Goodman et al. (1989b) who found that the Y-BOCS was significantly correlated with two independent measures of OCD. The same study also showed that the Y-BOCS is sensitive to changes in OCD symptoms. The Y-BOCS also has high internal consistency and high interrater 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
Goodman, W. K., Price, L. H., Rasmussen, S. A., Mazure, C., Fleischmann, R. L., Hill, C. L., … Charney, D. S. (1989a). The Yale-Brown Obsessive-Compulsive Scale. I. Development, Use, and Reliability. Archives of General Psychiatry, 46(11), 1006-1011.

Treatment



Radiosurgery ?

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

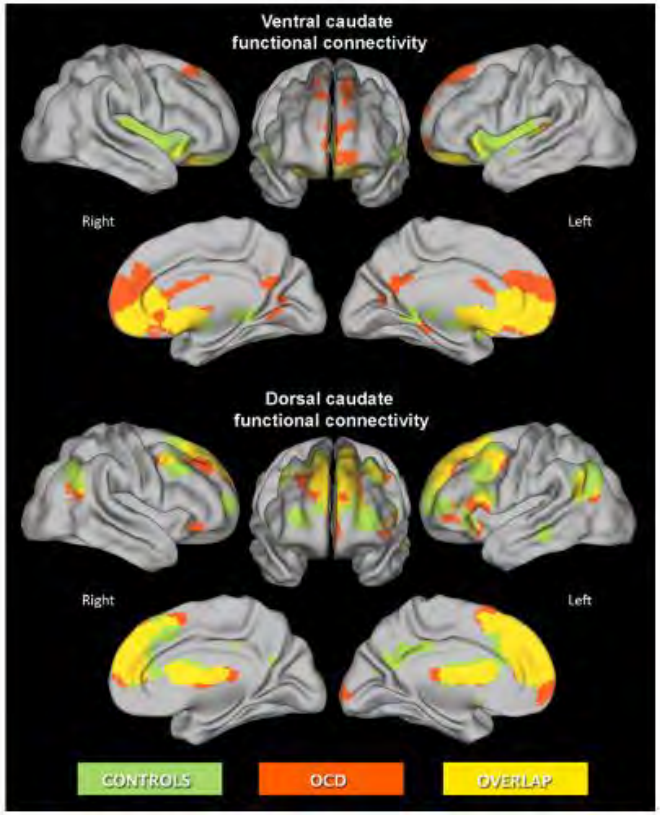
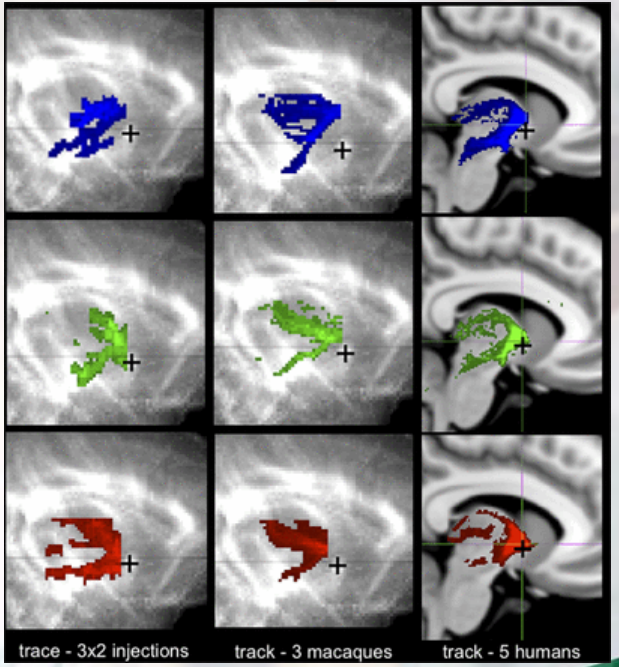


Figure 1. Significant within-group striatal functional connectivity maps in control subjects and obsessive-compulsive disorder (OCD) patients. Results are displayed on an inflated viewing of the cortical surface of the Population Average Landmark and Surface-Based Atlas (62).

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



Splitting of the trajectories from the lOFC, cOFC, and vmPFC in the IC into dorsal thalamic and ventral brainstem projections. In both species, the splitting occurs immediately caudal to the AC. Blue represents lOFC; green, cOFC; red, vmPFC. The black crosses represent the position of the AC

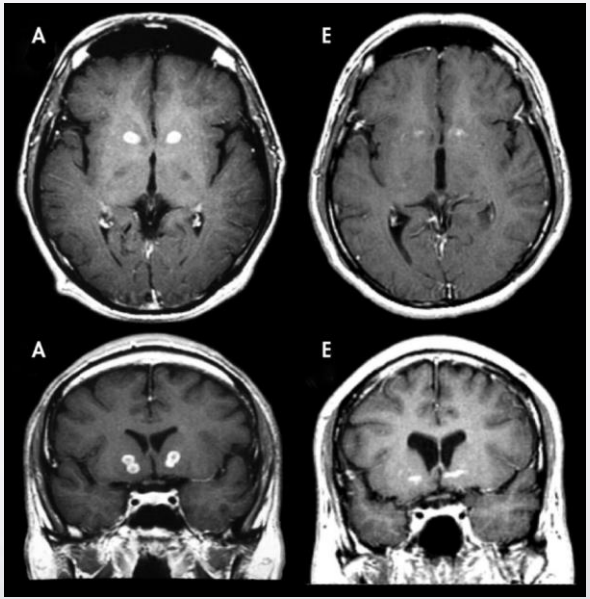
Journal of Neuroscience 13 February 2013, 33 (7) 3190-3201

Treatment of Resistant Obsessive-Compulsive Disorder With Ventral Capsular/Ventral Striatal Gamma Capsulotomy: A Pilot Prospective Study

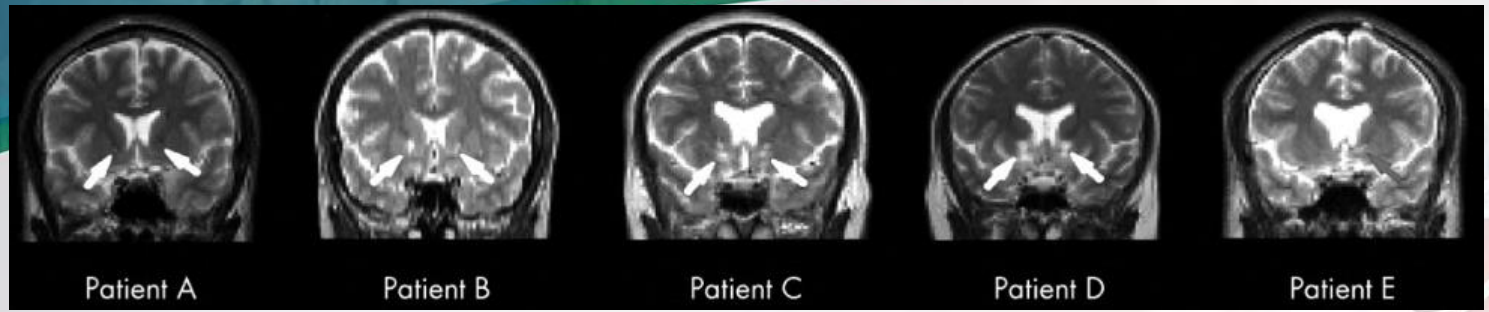
Antonio Carlos Lopes, M.D., M.Sc., Ph.D.
Benjamin D. Greenberg, M.D., Ph.D.
Georg Norén, M.D., Ph.D.
Miguel Montes Canteras, M.D., M.Sc.
Geraldo F. Busatto, M.D., Ph.D.
Maria Eugênia de Mathis, Psy.D.
Anita Taub, Psy.D., M.Sc.
Carina Chaubet D'Alcante, Psy.D.
Marcelo Queiroz Hoexter, M.D.
Fernando Sauerbronn Gouvea, M.D.
Janaína 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.

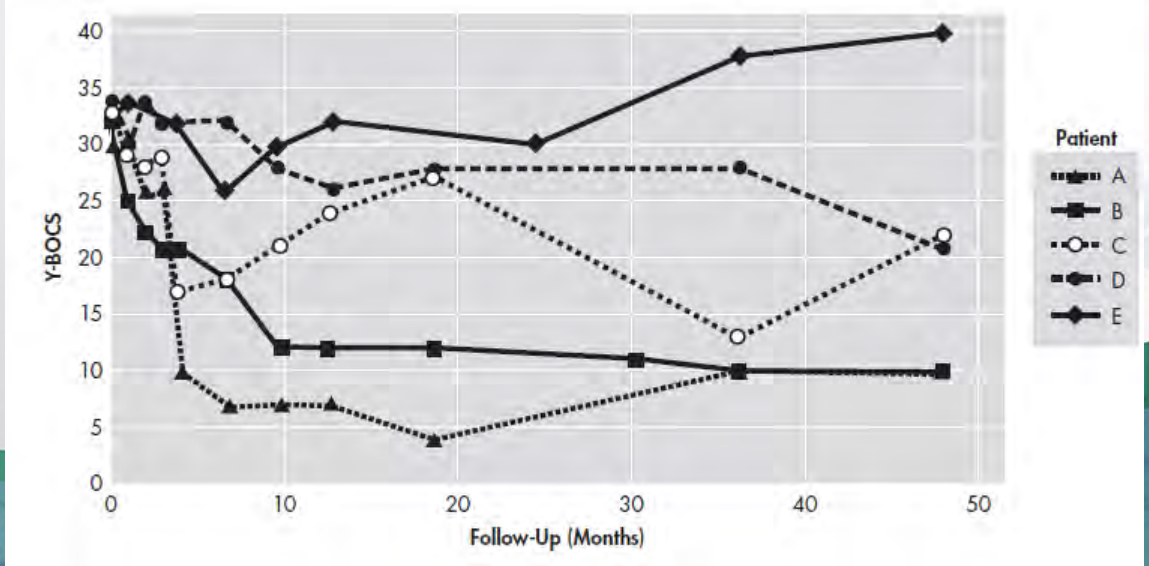
(The Journal of Neuropsychiatry and Clinical Neurosciences 2009; 21:381–392)



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



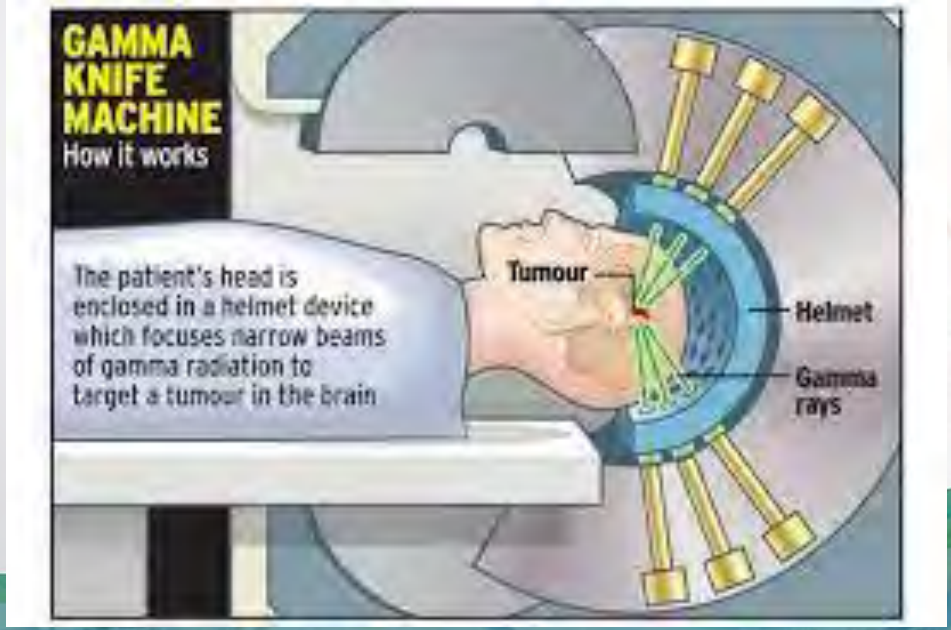
T2-Weighted Coronal MRI Slices Depicting Postoperative Ventral Capsular/Ventral Striatal Gamma Capsulotomy Lesions in 5 Patients



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

Author	Patient No.	Preoperative YBOCS	Last YBOCS	Follow-up, mo	Radiation Dose, Gy
Lopes[3]	1	30	10	48	180
	2	32	10	48	180
	3	33	22	48	180
	4	34	21	48	180
	5	32	40	48	180
Ruck[12]	1	28	24	156	200
	2	36	5	144	200
	3	38	28	84	180
	4	35	1	180	200
	5	27	15	180	200
	6	33	1	144	200
	7	39	35	12	180
	8	30	9	96	180
Kondziolka	1	34	24	55	140
	2	39	8	42	140
	3	39	18	28	150

[a]OCD, obessive compulsive disorder; YBOCS, Yale-Brown Obsessive Compulsive Scale.

Archival Report

Biological Psychiatry

Gamma Ventral Capsulotomy in Intractable Obsessive-Compulsive Disorder

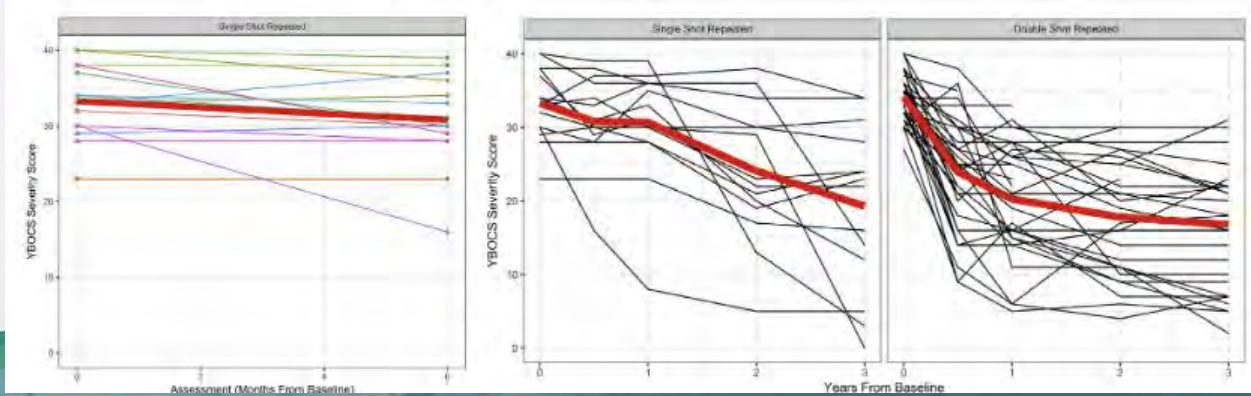
Steven A. Rasmussen, Georg Noren, Benjamin D. Greenberg, Richard Marsland, Nicole C. McLaughlin, Paul J. Malloy, Stephen P. Salloway, David R. Strong, Jane L. Eisen, Michael A. Jenike, Scott L. Rauch, Lee Baer, and Christer Lindquist

Biological Psychiatry Septemb

Table 4. Percent Decrease in Symptoms From Baseline to 6-, 12-, 24-, and 36-Month Assessments

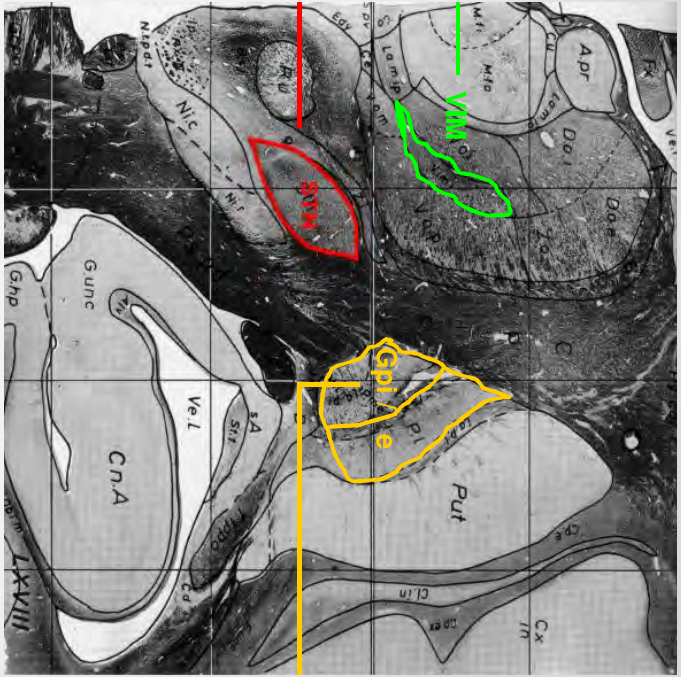
Time Since Surgery	<25%	25–34%	≥35%	*n*
Single Shot Repeated, *n* (%)[a]				
6 months	12 (80)	1 (6.67)	2 (13.33)	15
1 year	8 (53.33)	2 (13.33)	5 (33.33)	15
2 years	6 (40)	4 (26.67)	5 (33.33)	15
3 years	6 (40)	2 (13.33)	7 (46.67)	15
Double Shot, *n* (%)				
6 months	19 (47.5)	8 (20)	13 (32.5)	40
1 year	9 (22.5)	9 (22.5)	22 (55)	40
2 years	9 (22.5)	9 (22.5)	22 (55)	40
3 years	5 (12.5)	5 (12.5)	30 (75)	40

- 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)



Schaltenbrand Atlas

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 dosimetries
  - 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**

References

- De Toledo, Isabela Porto, et al. "Prevalence of trigeminal neuralgia: A systematic review." *The Journal of the American Dental Association* 147.7 (2016): 570-576.
- http://www.essentialtremor.org/wp-content/uploads/2013/07/FactSheet012013.pdf
- Louis, E.D., 2001. Essential tremor. New England Journal of Medicine,345(12), pp.887-891.
- 2012 - Brontë-Stewart - Deep brain stimulation - Neurol Clin Pract
- 2004 - Okun - Development and initial validation of a screening tool for PD surgical candidates - Neurology