Radiosurgery for functional disorders

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1951 (2 years after his stereotactic frame): Leksell conceive the idea of closed-skull, single-session irradiation of a precisely defined intracranial target. He applied this concept to functional neurosurgery and crossfired photon or proton radiation beams to obtain functional destruction of normal brain. To treat his initial few patients with trigeminal neuralgia, Leksell coupled an orthovoltage X-ray tube to his early generation stereotactic frame and subsequently tested a modified LINEAC.

1967: first Gamma functional radiosurgery tool with collimator helmets that created discoid shaped lesions that could “section” white matter tracts or brain tissue in a manner similar to a leucotome or other instrument. Subsequent refinements of the Gamma Knife provided more flexibility in the creation of lesions with different sized circular collimators.

Leksell; Acta Chir Scand; 1951; 102
Leksell; Acta Chir Scand; 1971; 137
Radiosurgery

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The Stereotaxic Method and Radiosurgery of the Brain.

By

LARS LEKSELL
Gamma Knife® evolution
Perfexion
Functional indications

Movement disorders
Behavioral disease
Epilepsy
Pain
Early experiences

First Leksell stereotactic frame for use with probes and electrodes, made it easily adaptable for cross-firing narrow beams of radiation, providing the basis for radiosurgery. The first attempt to subplant the electrodes with ionizing radiation was made in the early fifties, with X-rays, tempting to try to reduce the hazards of open surgery, by the administration of a single heavy dose of radiation and it appeared possible to destroy any deep brain structure. Ten years later physicists Kurt Liden and Borje Larsson: first proton beam operation in Uppsala. The heavy particle beam was an excellent knife blade but the synchro-cyclotron was too clumsy. Similar technique was developed for a linear accelerator.

Leksell; Journal of Neurology, Neurosurgery, and Psychiatry 1983; 46
First Gamma Knife®

Precise & simple tool which could be handled by the surgeon.

1968: first stereotactic Gamma Unit, using Cobalt 60, was installed at the Sophiahemmet Hospital and was primarily intended for functional indications.

The lesions were disc shaped and very sharply circumscribed.

1974: second Gamma Unit, with spherical fields of radiation, was installed at the Karolinska Hospital in Stockholm.

Many problems have been solved by the arrival of the new imaging techniques.

Leksell; Journal of Neurology, Neurosurgery, and Psychiatry 1983; 46
Initial functional experiences

Initially functional radiosurgery was performed for a limited number of patients with intractable pain related to malignancy, movement disorders, psychiatric illness, and trigeminal neuralgia.

Percutaneous retrogasserian glycerol rhizotomy was developed.

Radiosurgical hypophysectomy and medial thalamotomy for intractable cancer pain.

Doses in excess of 150 Gy provided reproducible small volume tissue necrosis. Early animal experiments showed consistent lesion creation at doses ≥ 150 Gy.

Kondziolka; Surg Neurol Int. 2012; 3(Suppl 1)
Gamma Knife indications
Thalamotomy for Parkinson disease or essential tremor. Ventralis intermedius (VIM) thalamic nucleus target. DBS is not always available. For radiosurgical thalamotomy imaging (contrast ventriculography > CT imaging > MRI) definition alone is used to determine lesion placement. Radiosurgical thalamotomy contralateral to a prior radiofrequency lesion or to enlarge a previous lesion. Pts older than in DBS. 20% isodose kept medial to the internal capsule. Beam blocking to restrict the dose toward the internal capsule. Differents gamma angles. Tremor relief in 76-93%. Mean time to improvement 2m. Complication (Pittsburg) 1.3%-7.7%. Dose range of 110–165 Gy (better results at higher doses).
Behavioral disorders

Several potential radiosurgery targets for behavioral disorders. Anterior capsulotomy in patients with medically refractory OCD. First radiosurgical capsulotomy performed by Leksell in 1953 using 300 kV X-rays. Pneumoencephalography for target definition; bilateral anterior internal capsule lesions. 5/7 pts long-term benefit after 7 years of follow-up. Since 1988 additional patients managed in Stockholm. Recommended use of only 4-mm isocenters. Pittsburg: bilateral oval lesions (two 4-mm shots) in the ventral capsule at the putaminal midpoint. Maximum dose 140–150 Gy. Other patients managed in Spain, Turkey and Brazil. The results seem to be as efficacious as radiofrequency lesions.

Kondziolka; Surg Neurol Int. 2012; 3(Suppl 1)
Epilepsy

Focal brain irradiation can lead to amelioration of seizures due to brain tumors, AVM and other pathologies. In 1985, Barcia-Salorio: 6 epileptic pts low-dose RS (10 Gy). Focus localized by EEG, subarachnoid & depth electrodes. In 1994 long-term analysis of 11 patients (dose 10–20 Gy): 5 pts had complete cessation of seizures and 5 improved. Seizures began to decrease after 3–12 m following RS. Lindquist and colleagues at the Karolinska Institute began to perform epilepsy RS using also MEG to define focus. Value in gelastic or generalized seizures in hamartomas. Amygdalohippocampal lesion for mesial temporal sclerosis as proposed by Regis: Gamma Knife conformal volume of radiation for the amygdala and hippocampus ($\approx 7$- ml, margin dose of 25 Gy to the 50% isodose line, a dose that later caused target necrosis. The first patient became seizure free immediately or latency of almost 1 year. Doses 10–100 Gy: typical 40–50 Gy to a volume less than 7.5 ml.
Case report by Leksell in 1968 and larger series by Steiner in 1980, after little has been written. Young et al. performed medial thalamotomy for chronic non-cancer pain: 2/3 of 41 pts had at least a 50% reduction. Pts with deafferentation pain responded poorly, but more encouraging results were identified in patients with nociceptive syndromes. Hayashi: pituitary gland-stalk ablation by GKRS, between pituitary stalk and gland (160 Gy and the 8-mm collimator) to control cancer pain; all the 9 patients became pain-free within a few days after radiosurgery. No patient developed panhypopituitarism and diabetes insipidus. This strategy of pituitary gland–stalk ablation for pain control also showed a good initial response (88%) of 8 patients with thalamic pain syndrome; however, the majority of patients (71%) experienced pain recurrence during the 6-month follow-up. Large amount of literature on SRS for trigeminal neuralgia.
Electricity and Pain

Mercury water and cauterizing stones: Nicolas André and tic douloureux

Brown (1999); J Neurosurg 90
Behavioral disease Planning

Single/Two 4 mm shot

50% isodose

130-150 Gy at maximum isodose
Movement disorders Planning

Single 4 mm shot

50% isodose

110–165 Gy maximum dose

Plugs

Target Volume = 92-93 mm$^3$
Epilepsy Planning

Multiple shots 50% isodose
10-50 Gy at prescription isodose
10-100 Gy at maximum dose
Plugging/Sectors to spare adjacent structures
“large” Target Volume $\approx 7$ cm$^3$
Intractable Pain Planning

Single shot 4/8 mm

50% isodose

150 Gy at maximum

“small” Target Volume
Trigeminal Neuralgia Planning

Single 4 mm shot
50% isodose
40-45 Gy at prescription isodose
80-100 Gy maximum dose
No plugs
Target Volume = 92-93 mm³
Trigeminal Neuralgia (TN)

Epidemiology:
4-5 new cases / 100,000 / year
25% became drug resistant
Usually old people
F > M
Diagnosys

Clinical History
Other neurological symptoms / signs
Blinking Reflex

Radiology
OPT/RX
MRI (CT)
Therapy

Practice Parameter: The diagnostic evaluation and treatment of trigeminal neuralgia (an evidence-based review)
Report of the Quality Standards Subcommittee of the American Academy of Neurology and the European Federation of Neurological Societies; Neurology 71 October 7, 2008
Therapy

Drugs
Carbamazepine - Oxcarbazepine
Lamotrigine / Baclofen
Clonazepam - Gabapentin - Fenitoina - Valproato

Anthalgic
Acupuncture, local anesthetic injection

Percutaneous rizotomy

MVD: the only etiological approach

Gamma Knife Radiosurgery
Gamma Knife RS for TN
Neuromodulation

Radiosurgery is commonly considered to be effective through a destructive physical mechanism acting on neural tissue. However, the results of modern neurophysiological, radiological, and histological studies are providing a basis on which to question this assumption. There are now multiple pieces of evidence pointing to a nonlesional mechanism of the radiosurgical action. It appears that tissue destruction is absent or minimal and in almost all cases insufficient to explain the clinical effects produced. There is a real possibility that radiosurgery induces changes in the functioning of neural tissue by differential effects on various neuronal populations and remodeling the glial environment, leading to modulation of function while preserving basic processing. Hence, the majority of radiosurgical procedures induce the desired biological effect without histological destruction of tissue. These findings may result in a major paradigm shift in the treatment of functional brain disorders.

Règis; Acta Neurochir Suppl. 2013;116
Team

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Case Mix 1993 – 2013 (6199 pts)

- Vascular: 46%
- Functional: 39%
- Benign Tumors: 10%
- Malignancies: 5%
Pain

308 Functional (5%)
  7 cluster headache
301 TN (97.7%)
  232 NV conflict
  32 idiopathic
  32 MS
  5 post-herpetic
  4 neoplastic
  2 scare related (post-surg)
  1 atypic
GKRS results

Symptomatic Approach
High efficacy (75-99%)
....but lost in time
69% at 1 y
52% at 3 y
6% hypoesthesia (up to 37%)
6% dysesthesia (max 13%)
No extratrigeminal complications
Efficacy: dose related

80% pain free a 70 Gy
93% pain free a 90 Gy
Up to 3m to became pain free
Must continue drug treatments
Hyo-disesthesia > 35 m
Indications

2/3 first Neurosurgical approach
1/6 one previous approach
1/6 multiple previous approach
MR modifications
Alternative Target
Sharp Dose fall off
Conclusions TN

Many publications attest the efficacy of Gamma Knife RS in TN

Non-invasive: elderly patients or co-morbidity

Patient choice
Conclusions Functional

Some well established indications (TN)

Movement Disorders Behavioral indications and Pain need a strong departimental multidisciplinary support, that can be reached only in extremely selected centers