Principles of Stereotaxy, Psychosurgery and Radiosurgery

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Part 1

Stereotaxy

Stereotactic vs. Stereotaxic

- 1908 – Victor Horsley and Robert Clarke introduced an apparatus that, by using a Cartesian coordinate system, allowed passage of a probe, blade or needle under accurate control into a subcortical structure of a monkey
  - They called it stereotaxic (stereos = three dimensional, taxus = an arrangement)
- 1973 – International meeting decided to change the name to stereotactic (tactus = to touch)
- Currently – It has been adopted that stereotaxic is used when referring to animals, and stereotactic when referring to humans

Concept

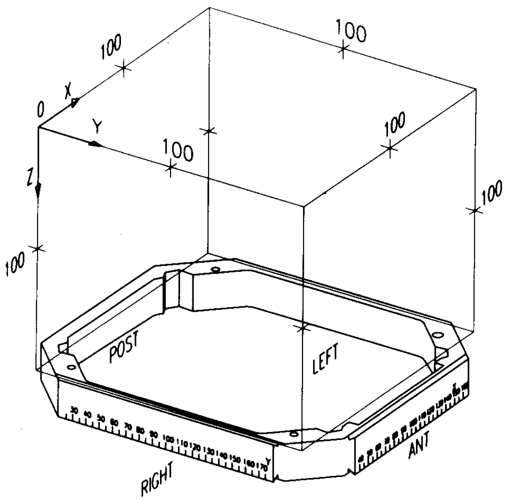
- Use images of the brain to guide the surgeon to a target within the brain by utilizing the stereotactic principle of co-registration of the patient with an imaging study
- This allows brain surgery to be accomplished with increased safety and smaller incisions by providing precise surgical guidance of the location of intracranial pathology
- This technique may utilize an external frame attached to the head (frame-based) or by imaging fixed landmarks or markers attached to the scalp (frameless or image guided surgery)

Leksell Frame (1949)

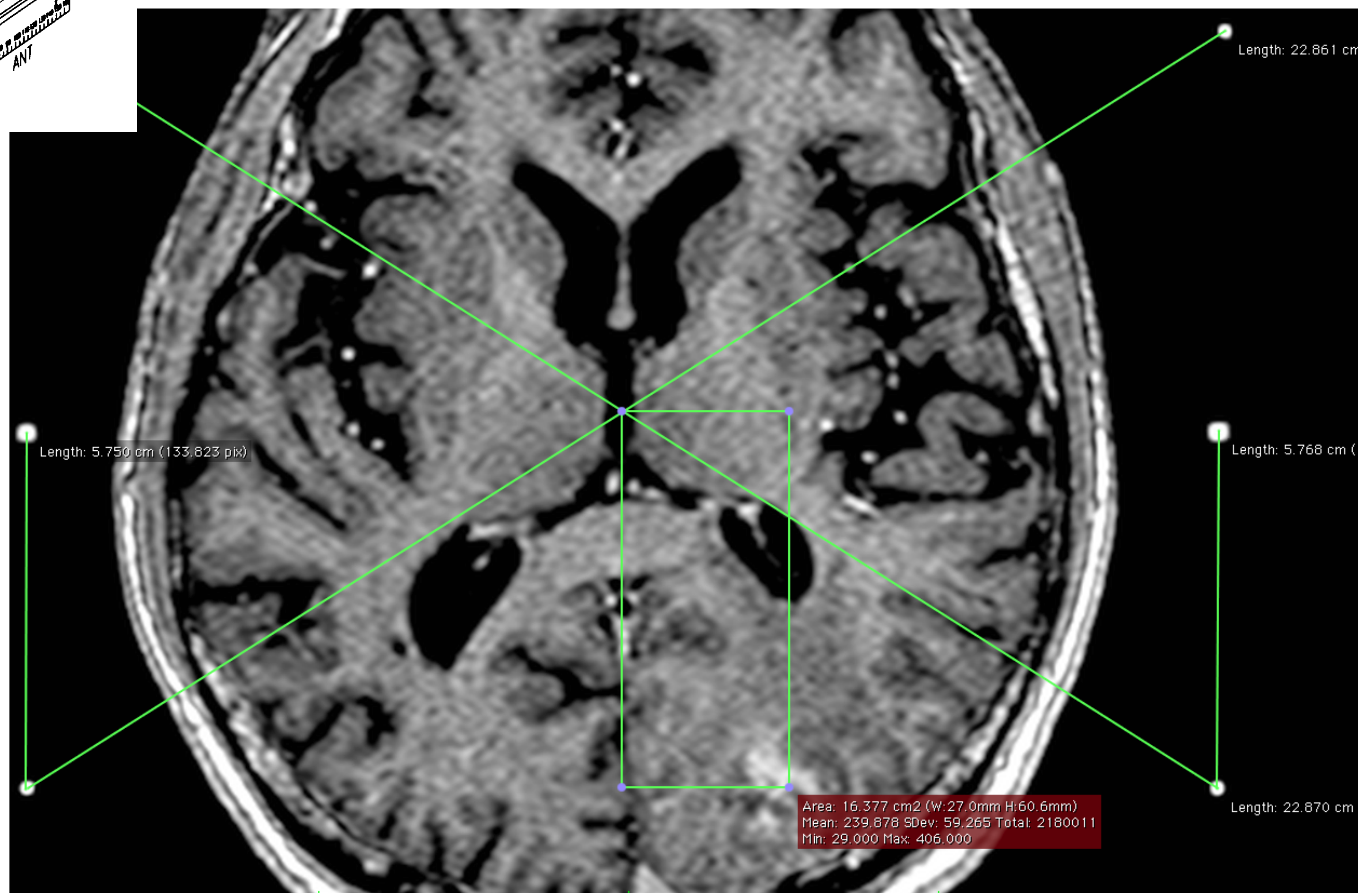
- Arc-centered design with movable probe carrier that rotates on a semicircular arc
- The carrier can be rotated in the left-right “arc” angle and in the AP “ring” angle
- The center of the frame and x,y,z coordinates is **100** and imaginary zero is at the superior, posterior, right side of the system

General Technique (Frame-based)

- Apply stereotactic frame using local anesthetic, then obtain CT or MR with the frame on
- Measure coordinates using the images for x and y axes. Use the separate z axis to determine depth
- Example...



X=00 Left (100+) / Right (100-)=00
Y=00 Ant. (100+) / Post. (100-)=00
Z=00 + 40 mm= 00



General Technique (Frameless)

- Apply fiducial markers to patient's head and obtain MR
  - Avoid placing markers in the same A/P or lateral plane
- Position patient in OR next to 3D digitizer, securely fix the head
- The device will locate a 3-dimentional point (triangular emitter mounted to the head clamp) and assign it a coordinate address
- Register the fiducials using the wand (defines the relationship between the space around the head and the MR image – i.e. localizer position is mapped onto the image space)

Why use Stereotaxy?

- Facilitates a precise planning of the craniotomy especially in cases of limited surgical exposure
- Facilitates a precise planning of the surgical vector to targeted small, subcortical lesions
- Minimizes invasiveness by more accurately selecting the best trajectory to the lesion
- Stereotactic biopsy of intracranial lesions
- Ensures more precise identification of normal structures for greater safety
- Helps to define the tumour margins and the limits of resection thereby guiding the complete removal of a lesion
- Useful in localizing encased and displaced vascular structures, the tumour extension into various brain crevices and the position of osseous landmarks

Common Uses of Stereotaxy

- Stereotactic brain biopsy. Deep tumors within the brain may be difficult and dangerous to approach by an open operation. Using a stereotactic biopsy apparatus fixed to the head frame and adjusted to the target coordinates, a biopsy probe is passed through a small hole in the skull to sample tissue for pathology.
- Placement of lesioning electrode for pallidotomies, thalamotomies etc.
- Placement chronic stimulation electrodes in the deep brain to treat movement disorders, such as Parkinson’s disease and essential tremor.
- Can make functional maps of subcortical structures using recording electrodes
- Shunt catheter placement
- Stereotactic radiosurgery

Principles of Frameless System

- **Important**: To calculate the mathematical relationship between the image volume and the surgical working space, a rigid body transformation has to be established.
  - In image-guided neurosurgery, this transformation is based on either point-pair matching or surface matching
    - Point-pair matching: corresponding fiducial points are defined in images and surgical space. A coordinate transformation is subsequently calculated to minimize the average residual distance between these corresponding fiducial points
    - Although point-pair matching based on bone screws (implanted fiducial markers) is generally accepted to yield the most accurate measurements, this method is often avoided in neurosurgical practice because of its invasiveness. Three alternatives to implanted fiducial markers are available: adhesive fiducial markers, anatomical landmarks, and surface matching.
    - Surface matching: a large number of points on the skin are digitized in the surgical working space. Again, a coordinate transformation is calculated to minimize the residual distance between each point in the surgical volume and the reconstructed skin surface in the image volume

Registration Methods

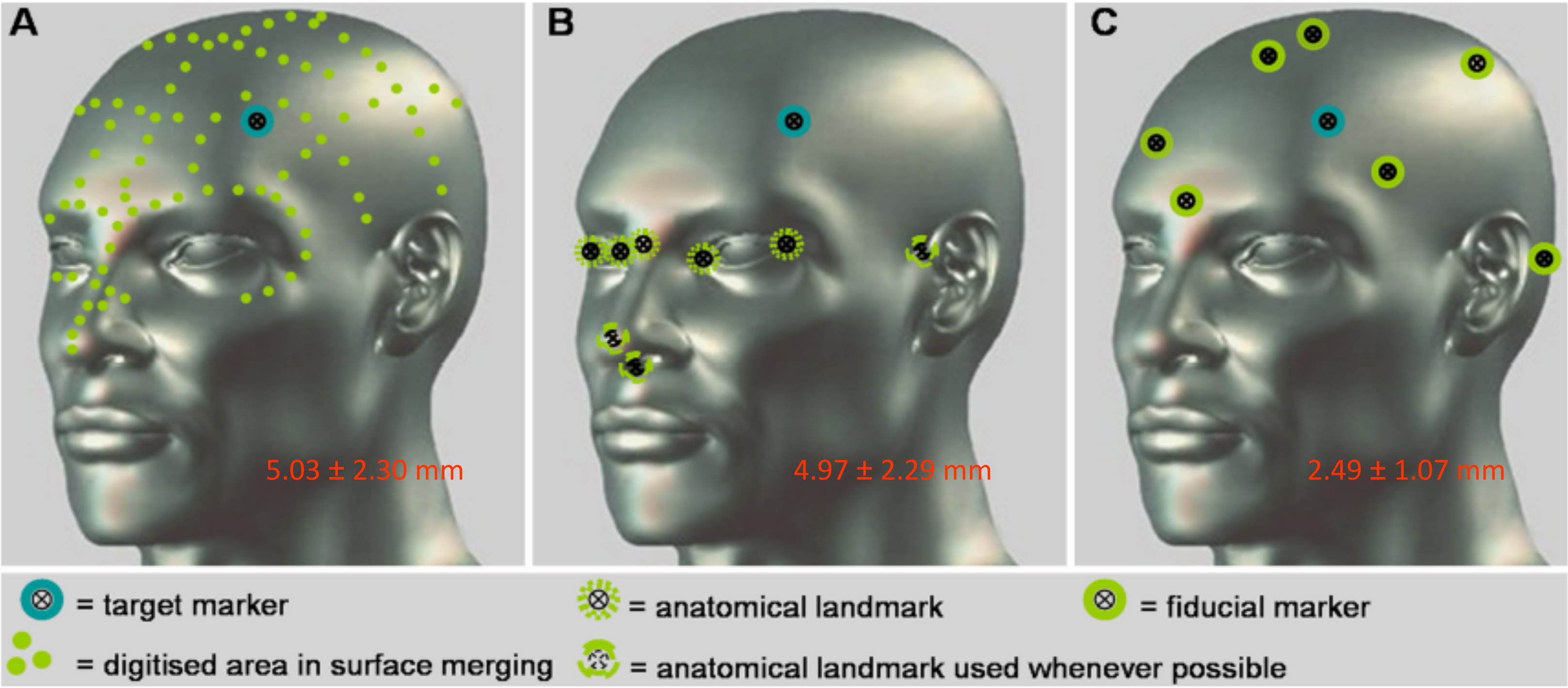


FIG. 2. Illustrations of typical configurations of registration points. A: Surface matching registration. B: Anatomical landmark registration. C: Adhesive fiducial marker registration. A target marker is also placed on the scalp (here in the left frontal region).

Error of localization (aka average distance between the probe and its intended target) = $([X_{is} - X_{ws}]^2 + [Y_{is} - Y_{ws}]^2 + [Z_{is} - Z_{ws}]^2)^{1/2}$ where is = image space and ws = world space

Comparison of Registration Methods

- Woerdeman *et al* 2007:
  - 50 patients underwent frameless guided procedures, performed all three methods of registration on each patient and compared error
  - Found that skin adhesive fiducial marker registration is the most accurate noninvasive registration method
  - When images from an earlier study are to be used and accuracy may be slightly compromised, anatomical landmarks and surface matching are equally accurate alternatives.

Error Semantics

- Intraoperative computer workstations provide an estimate of root mean square error (RMS) following coregistration of skin fiducials or the stereotactic headframe.
- However this value should not be considered indicative of true accuracy.
- Rather, RMS represents the degree of internal consistency between data points—in this case the computed coordinates within the virtual space of the computer workstation. (i.e. gives a root mean square difference of the distance between the position of a target in image space and the position reached by the stereotactic system when that target is digitized in world space)
- RMS gives no information regarding the correspondence of those coordinates to the actual location of objects in physical space.
- This should not be confused with the mean errors reported for individual axes in some studies which utilized planar imaging to measure targeting accuracy.
- In such instances mean errors refers to the average error within a single anatomic plane.
- A Euclidean error is then calculated as the square root of the sum of the squares of the mean errors in each dimension. Euclidean error is therefore generally larger than mean error, and more representative of the actual distance from a target one could reliably expect to achieve.

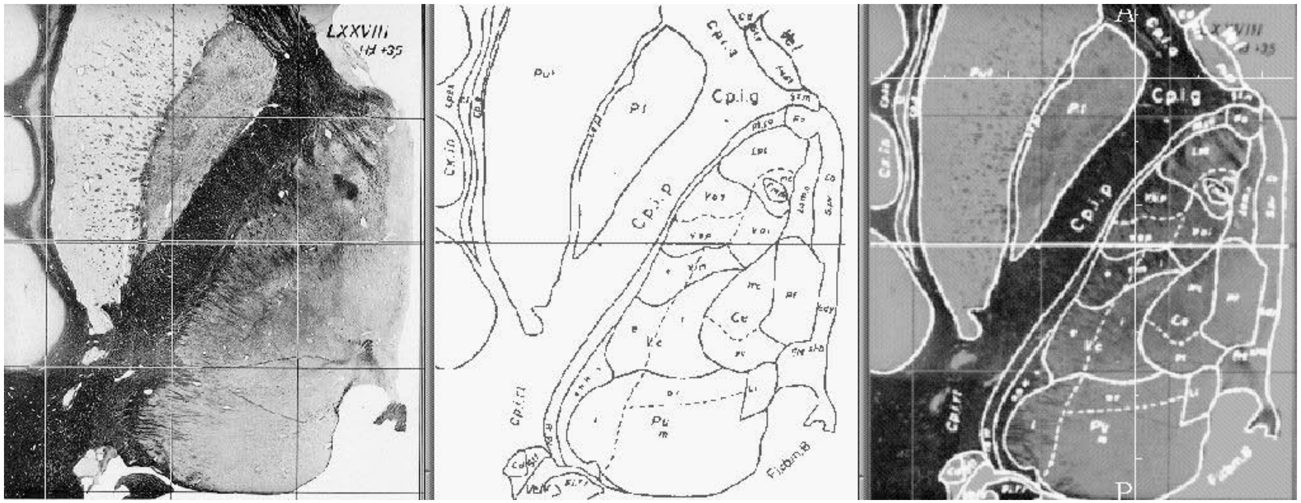
Sources of error

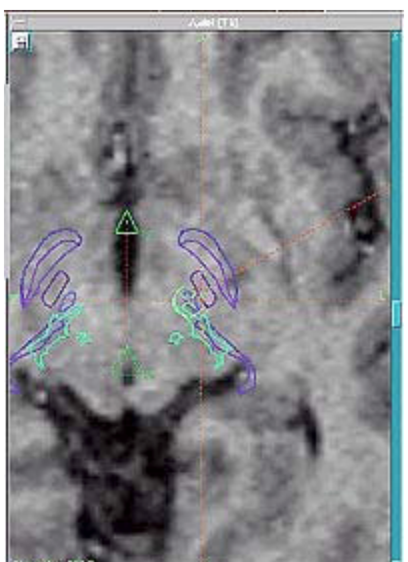
- Possible sources of error when using frameless image guidance:
  - Brain morphology changes throughout the operation
  - Registration error
  - Bent probe
  - Skin markers are mobile
  - Imprecise trackable probe positioning and computer cursor positioning
  - Accuracy varies throughout various locations in a given registered target volume (because location of the fiducials has a significant impact on the zone of maximal correlation)

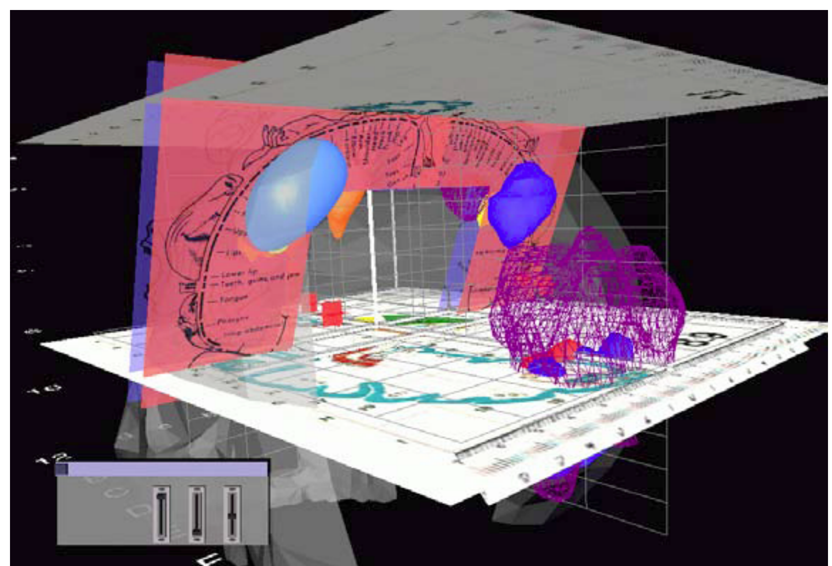
Frame-based vs. Frameless

- Smith 2005:
  - 213 consecutive stereotactic brain biopsies performed at UCSF (139 frame-based and 74 frameless)
  - There were no significant differences between the frame-based and frameless biopsy groups with regard to patient demographics, overall histopathology, proportion of nondiagnostic biopsies, or incidence of complications
  - The frame-based approach, however, required significantly less anesthesia resources, less operating room time and shorter hospital stays
  - (note: most frameless biopsies done under GA)

Brain Atlases







Brain Atlases

- Overall, tend not to be specific enough
- In practice, use imaging/atlases to localize the tentative target, then use physiological monitoring to confirm (insert electrode and record listening for potentials)
- DBS or RF lesion placed based on physiologic monitoring

Part 2

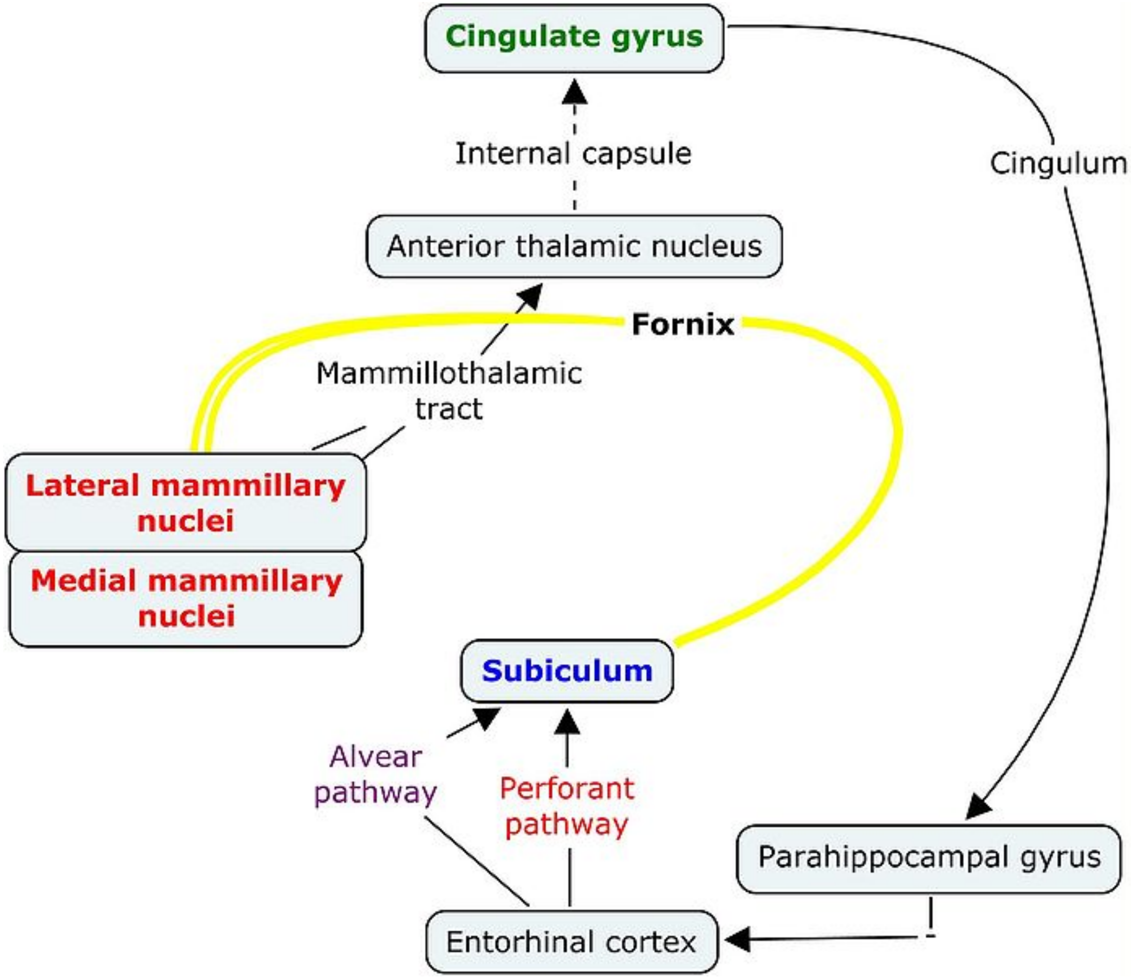
Psychosurgery

Egas Moniz **Almeida Lima**

Background

- 1937
  - James Papez, an American neuroanatomist, described the Papez circuit as one of the major pathways of the limbic system chiefly involved in the cortical control of emotion.
  - Papez discovered the circuit after injecting rabies virus into a cat's hippocampus and monitoring its progression through the brain.
- 1950’s
  - Paul Maclean, a neuroscientist at Yale, expanded on the concept of the Papez circuit to include the prefrontal cortex and the amygdala

Papez Circuit – a proposed mechanism of emotion



History

- Late 1800's
  - Gottlleb Burckhardt performed the first topectomies on 6 patients considered to be mentally ill (defined as dementia and paranoia)
  - Created specific lesions in the frontal and temporal regions of the brain to overall alleviate symptoms
  - The results from these operations ranged from reducing levels of excitement and violence to the death of one patient a few days after the operation

History

- 1935
  - Egas Moniz, a distinguished Portuguese neurologist and the discoverer of cerebral angiography, had his neurosurgeon, Almeida Lima, perform the first surgical intervention for the treatment of mental illness
  - The initial procedure involved injection of alcohol into the frontal lobes and was named ”prefrontal leukotomy,” becoming the first valid attempt in the surgical treatment of mental diseases
  - Published the findings of 20 leukotomies of the frontal lobe
    - Results: 1/3 of patients markedly improved, 1/3 minimally improved, and 1/3 showed no change in alleviating their illnesses
  - The neurosurgical treatment of psychiatric illness had thus begun and the term *psychosurgery was coined to describe this novel approach*
  - Moniz received the Nobel Prize in 1949 for his contributions in the field of psychosurgery and for his study on the functions and physiology of the frontal lobes

History

- 1940's and 50's
  - Leukotomy soon became known as lobotomy in the United States and was advanced further by neuropsychiatrist Freeman and neurosurgeon Watts, who developed the trans-orbital leukotomy (ice-pick lobotomy)

History

- 1950’s
  - Lithium and Chlorpromazine discovered leading to fewer individuals being institutionalized
- 1960’s
  - People starting to question the ethics of psychosurgery
- 1970’s
  - US legislation passed emphasizing the importance of using ethical boards regarding the selection of patients and the protection of human subjects
- 1980’s
  - Shift from ablative procedures to stimulation (DBS)
- Currently
  - Psychosurgery used for those with intractable psychiatric illness in whom medications have failed
  - Mainly used in refractory Obsessive Compulsive Disorder and severe Major Depressive Disorder

Criteria for Surgery

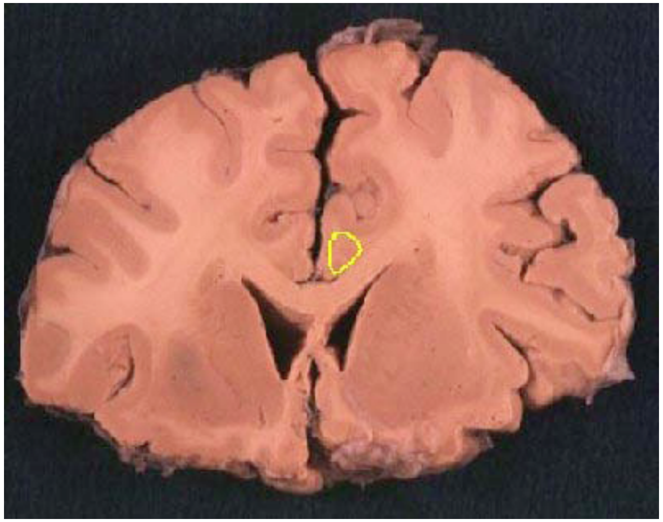
- Must fulfill DSM-IV criteria for the psychiatric disorder
- Severe illness defined by scoring systems (eg. Yale Brown OCD Scale, or YBOCS)
- Significant reduction in psychosocial functioning
- Patients themselves must provide consent
- Failure of adequate trial of therapy (usually at least 5 years of intensive psychiatric therapy)
- Each case is reviewed by a multidisciplinary review committee
  - Neuropsychiatry, Neurosurgery, Clinical Psychology, Hospital Ethics, Social Work

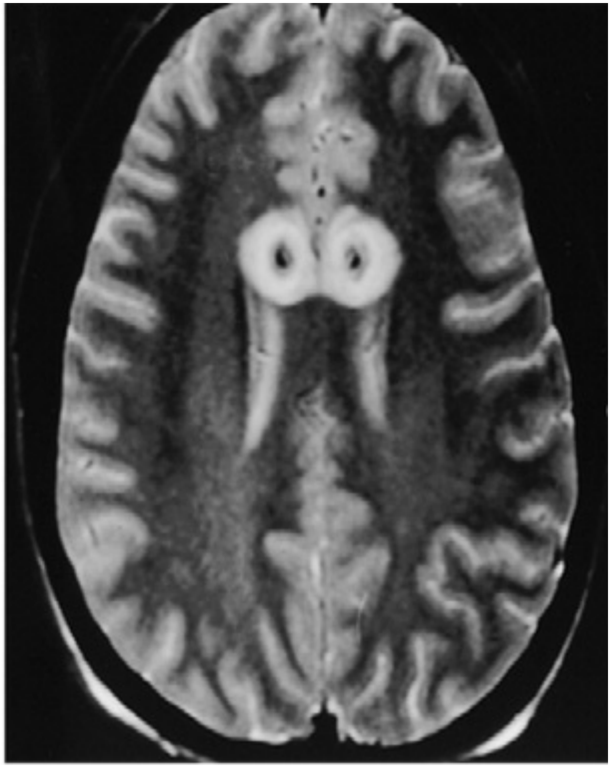
Current Procedures

- Cingulotomy
- Capsulotomy
- Subcaudate tractotomy
- Limbic leukotomy

Cingulotomy

- 1 cm bilateral lesions of the cingulum using thermoregulation
- Target:
  - 20 mm posterior to anterior-most tip of frontal horn and 7mm lateral to midline





Cingulotomy - Evidence

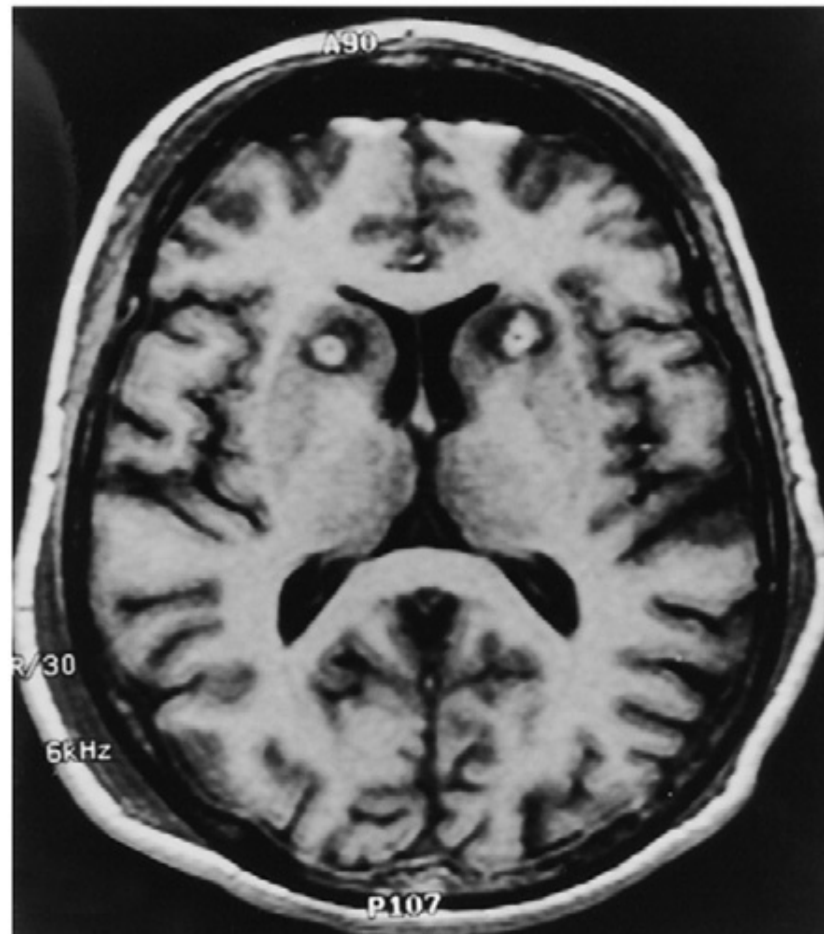
- Dougherty et al (2002)
  - Prospective study of 44 patients with refractory OCD
  - Patients underwent one or more cingulotomies
  - 6-month follow-up
    - 45% of patients responded at least partly to the therapy, specifically 20 patients after one cingulotomy and 7 of the 18 patients who undertook multiple cingulotomies

Capsulotomy

- Lesions created in the anterior limb of the internal capsule to interrupt pathways between the thalamus and the orbitofrontal cortex
- These lesions focus specifically on providing therapy for illnesses such as generalized anxiety disorder and OCD

Capsulotomy

- Target:
  - anterior limb of internal capsule
  - 5mm behind tip of frontal horn, 20 mm lateral or halfway between frontal horn tip and foramen of Munro
  - At level of foramen of Munro
  - At the border between putamen and pallidum



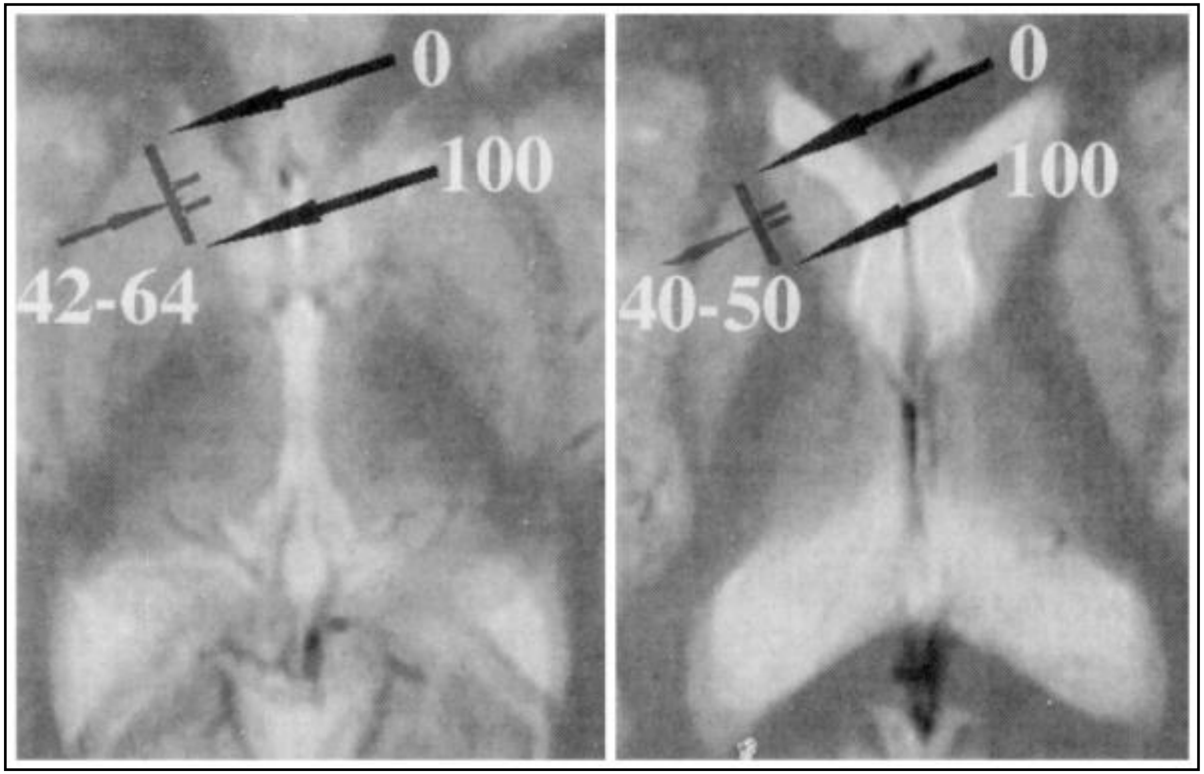
Capsulotomy Evidence

- Lippitz et al (1999)
  - OCD patients in Sweden, 22 underwent bilateral thermocapsulotomy (n = 22) or radiosurgical gamma knife capsulotomy (n = 13)
  - Results:
    - A right-sided anatomically defined lesion volume was identified in all successfully treated patients.
    - This common topographic denominator was defined in the approximate middle of the anterior limb of the internal capsule on the plane parallel to the anterior commissure-posterior commissure line at the level of the foramen of Monro and 4 mm above on the plane defined by the internal cerebral vein.
    - This region was unaffected in patients with poor outcomes. On the left side, no particular lesion topography was associated with clinical outcome

Capsulotomy - Evidence

- Rück et al (2003)
  - 26 individuals mostly with general anxiety disorder, some with panic disorder and social phobia, all refractory to both pharmacologic and psychological treatment
  - 50% of subjects showed an overall reduction of symptoms with no statistical significance between the different diagnoses involved in the study
  - Adverse outcomes occurred after surgery, such as one patient committing suicide and a few patients with a decline in daily functioning
  - Despite the studies that have occurred, capsulotomy may be helpful in the treatment of patients with treatment-resistant anxiety disorders

FIGURE 1



Lesion topography and outcome after thermocapsulotomy or gamma knife capsulotomy for obsessive-compulsive disorder: relevance of the right hemisphere.
Lippitz BE; Mindus P; Meyerson BA; Kihlstrx00F6;m L; Lindquist C

Neurosurgery. 44(3):452-8; discussion 458-60, 1999 Mar.

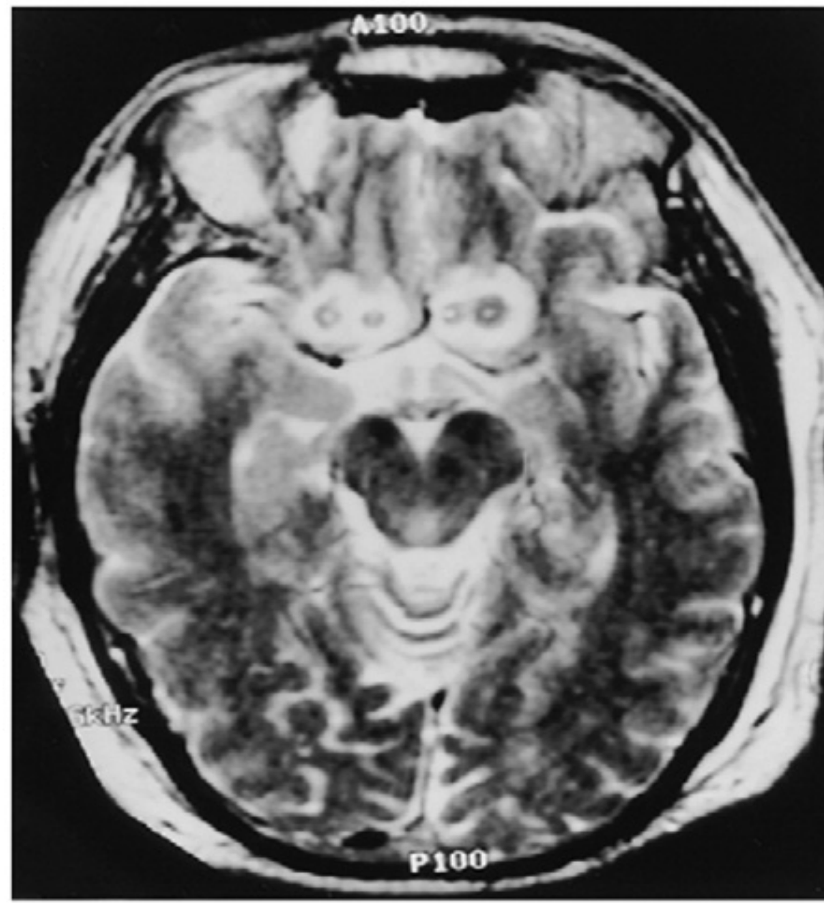
FIGURE 1 . Demonstration of the lesion definition within the anterior limb of the internal capsule; the lateral edge of the putamen was assigned to constitute the 0 coordinate, and the capsular part adjacent to the medial putaminal edge was defined as the 100 coordinate. The common topographic denominator of cases with good outcomes could be defined on the plane at the level of the foramen of Monro (coordinate, 42-64) and approximately 4 mm above on the plane defined by the the internal cerebral vein (coordinate, 40-50).

Subcaudate Tractotomy

- Bilateral lesions produced anterior to the caudate nucleus, affecting the limbic loop of Papez
- Overall goal is to construct orbitofrontal lesions to modify the mood, while sparing alterations involving intellect

Subcaudate Tractotomy

- Target:
  - Ventral to caudate head = substantia innominata (15 mm lat, 10 mm dorsal to planum sphenoidale)
  - Intra-operative stimulation produces autonomic responses



Subcaudate Tractotomy - Evidence

- Only procedure performed at the Geoffrey Knight Unit in London where nearly 1300 operations have taken place since 1961 (Bridges et al 1994)
- Consequently, 40% to 60% of the patients ultimately live normal or near normal lives, while continuing medications in some instances
- There was also a reduction of suicide rate to 1% postoperatively, compared to 15% in cases of uncontrolled affective disorders
- Considered to be the last resort for treatment, no controlled trial against a comparable treatment is possible
- However, it appears reasonable to offer this procedure to patients with suicidal and deluded depression or with frequently swinging moods, not responding to other treatments

Limbic Leukotomy

- Combination of cingulotomy and stereotactic subcaudate tractotomy
- Used for OCD

Limbic Leukotomy - Evidence

- Montoya et al (2002)
- 21 patients underwent limbic leukotomy, average postoperative follow-up period 2 years
- Side effects included headaches, seizures, and wound infections
- Found 36% to 50% of patients were considered responders, alleviating symptoms and ultimately improving their global functioning

Role of DBS in Psychosurgery

- Yet to be defined
- Greenberg et al (2006)
  - 4 Electrodes placed in ventral striatum and the anterior internal capsule
  - Used in 10 individuals with refractory OCD
  - Activation of the DBS was performed 3 weeks later
  - Patients then monitored every few months to determine the level of symptoms using the Y-BOCS scale
  - After following most of the individuals for 3 years, the results gathered showed that there was an overall 25% reduction of severity with the illness
  - Side effects included surgical complications, one instance of an intracranial hemorrhage, and one intraoperative seizure
  - Despite these effects, DBS appears to be more of a benefit to refractory psychiatric illness. However, as there was a development of adverse effects seen within patients who experienced DBS, the promising benefits of therapy demonstrate a need for further development in treating refractory psychiatric illnesses.

- Lozano et al (2008)
  - Background: subgenual cingulate region (Brodmann area 25) is metabolically overactive in treatment-resistant depression
  - Study: 20 patients with treatment resistant depression given DBS of subcallosal cingulate gyrus
  - Results:
    - There were both early and progressive benefits to DBS.
    - One month after surgery, 35% of patients met criteria for response with 10% of patients in remission.
    - Six months after surgery, 60% of patients were responders and 35% met criteria for remission, benefits that were largely maintained at 12 months.
    - The number of serious adverse effects was small with no patient experiencing permanent deficits.
  - Conclusions: This study suggests that DBS is relatively safe and provides significant improvement in patients with TRD

- Malone et al 2009
  - 15 patients with chronic, severe, refractory depression received DBS of ventral capsule/ventral striatum (VC/VS)
  - Electrodes were implanted bilaterally in the VC/VS region.
  - Stimulation was titrated to therapeutic benefit and the absence of adverse effects.
  - All patients received continuous stimulation and were followed for a minimum of 6 months to longer than 4 years.
  - Outcome measures included the Hamilton Depression Rating Scale-24 item (HDRS), the Montgomery-Asberg Depression Rating Scale (MADRS), and the Global Assessment of Function Scale (GAF).
  - RESULTS: Significant improvements in depressive symptoms were observed during DBS treatment.
    - Mean HDRS scores declined from 33.1 at baseline to 17.5 at 6 months and 14.3 at last follow-up.
    - Similar improvements were seen with the MADRS (34.8, 17.9, and 15.7, respectively) and the GAF (43.4, 55.5, and 61.8, respectively)
  - CONCLUSIONS: Deep brain stimulation of the VC/VS offers promise for the treatment of refractory major depression.

Part 3

Radiosurgery

Definition

- Stereotactic radiosurgery (SRS): precise delivery of a single, high dose of radiation in a one-day session
  - Multiple beams precisely collimated to the target inside the cranium
  - Limited to head and neck because these areas can be immobilized with skeletal fixation devices
  - 1 extremely high dose
  - Ablative, like surgical excision
  - Same day planning and treatment
  - Best for AVMs, benign lesions, and functional neurosurgery
- Fractionated stereotactic radiotherapy: several treatments are administered over a period of days or weeks with the assistance of removable masks and frames that achieve a lesser degree of immobilization.
  - Preferentially spares late responding/normal tissue resulting in higher therapeutic gain
  - Similar to true radiation therapy
  - Best for malignant tumours
- For the most part, stereotactic radiosurgery is limited to the head and neck, because these areas can be immobilized with skeletal fixation devices that completely restrict the head's movement, permitting the most precise and accurate treatment.

How it works

- The same as other forms of radiation
  - Distorts DNA of tumour cells, causing them to lose the ability to reproduce and retain fluid.
  - In AVMs, causes blood vessels to thicken and close off.
  - The shrinking of a tumour or closing off of a vessel occurs over a period of time.
    - For benign tumours and vessels, this will usually be 18 months to two years.
    - For malignant or metastatic tumours, results may be seen in a few months, because these cells are very fast-growing.

Types

- Particle beam (proton)
- Cobalt-60 based (photon)
  - Gamma Knife
- Linear accelerator based (linac)

Particle Beam

- First done in 1957
- Because protons have mass (cf. photons), speed can be controlled to minimize adjacent tissue injury
- The beam will stop at a depth related to the beam’s energy, therefore removing the exit dose
- Only available at a limited number of centres due to very high cost

Gamma Knife

- First prototype by Leksell and Larson 1967
- Uses relatively hemispherical array of multiple fixed cobalt-60 beams that are sharply collimated to create small, relatively spherical treatment volumes of varied diameter with sharp dose falloff

Linac

- First appeared in the 1980's
- High energy x-ray
- Good for treating large tumour volumes (>3.5cm) over several sessions
- Conformity of LINAC-Based Stereotactic Radiosurgery Using Dynamic Conformal Arcs and Micro-Multileaf Collimator
- Eg. Novalis Tx

Tomotherapy

- “Slice” therapy using CT images with Linac
- Unlike traditional radiotherapy systems with a slow moving external gantry designed for positioning individual beams onto the tumour from a few different directions, tomotherapy rapidly rotates the beam around the patient, thus allowing it to enter from many different angles in succession
- Beam intensity modulation is possible through the use of a multifleaf collimator system

Radiosensitivity

- The ability of normal tissue to tolerate radiation without injury depends on:
  - Radiation dose
  - Volume of tissue irradiated
  - Sensitivity of tissue affected
  - History of prior radiation treatment to the region
  - Individual variation between people

Indications

- AVMs
- All benign brain tumours including
  - Acoustic neuromas
  - Meningiomas
  - Pineal and pituitary tumours
- All malignant brain tumours including
  - Glial tumours and astrocytomas
  - Low grade tumours
- Metastatic brain tumours
- Functional disorders
  - Trigeminal neuralgia
  - Essential tremor
  - Parkinson’s

Radiosurgery vs. Surgery

- Auchter et al (1996)
  - multi-institutional retrospective study
  - patients with solitary brain metastases meeting the criteria for surgery of Patchell but treated with radiosurgery (Linac) combined with WBRT
  - Outcomes similar to those of patients treated with surgical resection combined with WBRT

Radiosurgery vs. WBRT

- Sneed et al (1999)
  - retrospective analysis of survival and local control in patients with brain metastasis treated with radiosurgery alone versus radiosurgery (Linac) plus WBRT
  - Survival and local control were the same for both groups. Regional control was better in the WBRT group; however, new metastatic lesions could be successfully salvaged with repeated radiosurgery treatments, leading to good intracranial control rates in both groups.
  - Concluded that if the treatment team was committed to using repeat radiosurgical treatments for new brain lesions, excellent overall brain control can be achieved without the need for WBRT

Radiosurgery Dosing (Shaw et al 2000)

Maximum tolerated dose of single fraction radiosurgery	Maximum tumour diameter
24 Gy	<20mm
18 Gy	21-30mm
15 Gy	31-40mm

- Unacceptable CNS toxicity was more likely in patients with larger tumours, whereas local tumour control was most dependent on the type of recurrent tumour and the treatment unit.

Radiosurgery Dosing

- Vogelbaum et al (2006) Local control of brain metastases by stereotactic radiosurgery in relation to dose to the tumor margin
  - *Objective:* The maximal tolerated dose (MTD) for stereotactic radiosurgery (SRS) for brain tumors was established bythe Radiation Therapy Oncology Group (RTOG) in protocol 90-05, which defined three dose groups based on the maximal tumour diameter. The goal in this retrospective study was to determine whether differences in doses to the margins of brain metastases affect the ability of SRS to achieve local control.
  - *Methods.*202 patients harbouring 375 tumours that met study entry criteria underwent SRS for treatment of one or multiple brain metastases. The median overall follow-up duration was 10.7 months (range 3–83months). A dose of 24 Gy to the tumour margin had a significantly lower risk of local failure than 15 or 18 Gy (p =0.0005; hazard ratio 0.277, confidence interval [CI] 0.134–0.573), whereas the 15- and 18-Gy groups were not significantly different from each other (p = 0.82) in this regard. The 1-year local control rate was 85% (95% CI 78–92%) intumors treated with 24 Gy, compared with 49% (CI 30–68%) in tumors treated with 18 Gy and 45% (CI 23–67%) intumors treated with 15 Gy. **Overall patient survival was independent of dose to the tumour margin.**
  - *Conclusions.* Use of the RTOG 90-05 dosing scheme for brain metastases is associated with a variable local control rate. Tumours larger than 2 cm are less effectively controlled than smaller lesions, which can be safely treated with 24 Gy

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