Gamma Knife Radio Surgery
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Principle:

GKRS:
- Stereotactic Radiosurgery (SRS)
- Radiosurgery involves the delivery of a single very high dose of radiation to a small and often critically located intracranial target through an intact skull.
- It uses gamma rays generated by the radioactive decay of Cobalt 60 delivered through 192 individual beams which intersect at a single spot with great precision and accuracy.
- It is an alternative AND/OR an adjunct to open surgery and conventional linear accelerator radiation therapy.
Lars Leksell (1907–1986) is considered the father of SRS.

He was a neurosurgery professor at the Karolinska institute in Stockholm, Sweden.

First Gamma Knife Prototype 1967.

History:

What happened to Dr Banner to turn him into the Incredible Hulk?
What is Radiation

- Electromagnetic Energy $E=hf$

- Many Forms
  - Photons Uncharged
  - X-rays
  - Gamma Rays Product of nuclear decay - Cobalt 60.
  - Protons + Charge
  - Electrons - Charge
  - Beta Particles
  - Alpha Particles

Radiation Therapy

- Discovery of x-rays in November 1895 by William Roentgen

- 3 weeks later radiation was used as a treatment for cancer.

- 3 years (1899) later reports appeared of “cure” in head and neck cancer.

Radiation Therapy

- Initially given in single session.

- Poor outcomes and horrendous side effects

- Primarily palliative in nature

- Generally used radioactive sources,
  - Radium
  - Cobalt
Radiobiology

- The study of the effects of radiation
- The science of how radiation works
- Explains the observations in clinical practice
  - Early effects: skin reaction, mucositis
  - Late effects: fibrosis, 2nd malignancies

How does it work ???

- Radiation inflicts unrepairable DNA damage leading to cell death at the next mitosis. Reproductive death.
- Single Strand vs Double Strand
- Base Excision vs Nucleotide Excision
- There is a period of time from treatment to effect.
Radiation Therapy Effects

- Acute & Chronic
  - Most concerned with chronic effects - irreversible
- Volume related
  - Increased volume -> increased effects
- Dose related
  - Increased dose -> increased effects
- Now Quantified
  - Dose limits/constraints are now well defined to minimize risk.
  - Specific to each organ
    - Lung/Kidney/Skin

Radiation Therapy

- Initially radiation therapy employed Cobalt or radium delivered through a collimator.
- With the advancement of technology linear accelerators were born.
- Radioactive sources were not necessary.
  - Hazardous
  - Safety hazard
  - Decayed
Contemporary Radiation Therapy

- Multidisciplinary
- Physicians
- Nurses
- Physicists
- Dosimetrists
- Therapists
- Radiation Safety
- Radiobiologists
- Biomedical engineers

The History of Radiation

- To truly appreciate the present we must look backward from where we have come. Let's look at our music.
- I phones
- I Pods
- CDs
- Cassettes
- Records
  - Bonus question: What were the 3 speeds on a record player?

Treatment

- Two Dimensional treatment
- Based on boney anatomy
- Large fields
- Large Shotgun effect – No sparing of normal tissues
Treatment

- Three Dimensional
- Employed CT images to define individual anatomy.
- Increased sparing of normal tissue
- Improved outcomes
- Less side effects
Stereotaxis

- The ability to define all points in a 3 dimensional volume.
- Each point has a unique x,y,z coordinate.
- With precise localization treatment volumes shrink dramatically and dose escalation is possible since all we are treating is the target/tumor. There is very little, or no, normal tissue within the treated volume.
**What is the Gamma Knife?**

- Radiation therapy delivered to intracranial tumors with extreme accuracy and precision.
- The Gamma Knife is the “sniper” of radiation therapy.
- Delivers VERY HIGH radiation doses to VERY SMALL targets.
- Uses radioactive Cobalt –60 as Gamma Ray source.

**Cobalt Decay**

\[ ^{60}_{27}\text{Co} \rightarrow ^{60}_{28}\text{Ni}^* + e^- \rightarrow ^{60}_{28}\text{Ni} + \gamma\text{-photon} \]

**Diagram:**

- Radiative cobalt
- Gamma rays
- Beam
- Target
- Delivery of radiation
**Principle of GKRS:**
- Conventional radiation therapy delivers small fractional doses over a longer period of time. The volume of radiation often can include a significant amount of normal brain tissue which is exposed to the same dose of radiation as the tumor target.
- Using stereotactic techniques, GKRS employs 192 beam paths (192) arranged to converge on the target creating a high dose of radiation in the target area while delivering a very small dose of radiation to the surrounding structures.

**Why use the Gamma Knife?**
- **Designed specifically for intracranial targets.**
- Traditional radiation techniques may result in neuro-cognitive changes in people who are long term survivors.
- The volume of normal brain tissue is dramatically reduced -> fewer side effects
- Dose escalation – more likely to eradicate disease
- Does not exclude future treatments if necessary such as whole brain radiation.

**Gamma Knife Advantages**
- Single Session (4 hr)  Treatment generally < 1 hr
- Accuracy/Precision.  <0.1 mm
- Little acute effects
- Long Term evidence confirming effectiveness.
- Limited late effects
- Dedicated solely to intracranial disease
- Non-Invasive.
- Unlikely to delay systemic therapy.
- Can be repeated.
Gamma Knife Disadvantages

- Size limitations at around 3 cm.
- Source Decay – Cobalt 60 half life of 5.26 years
- Single fraction is not ideal for locations close to critical structures and may increase risk of complications. Fractionated treatment is better choice.
- Regulatory and Safety requirements increased
- Exchange of sources is expensive and a homeland security issue. Initial source strength 6000 Curie!!!!
- Requires a large referral base to be viable.
- Only treats intracranial disease.

Principle:

Which Angel had Cancer?
Indications:

- OVER 884,000 PATIENTS TREATED THROUGH 2014, WORLDWIDE

Treatment steps:

- Step 1: Placement of the head frame

Treatment Steps

- Frame Placement
- Neuroimaging
- Treatment Planning
- Treatment
- Frame Removal
Treatment steps:

- Step 1: Placement of the head frame

Frame Placement

- The frame defines the "surgical volume".
- Secured to the skull by 4 non-metallic pins.
- Placed by Neurosurgeon after sedation and local anesthesia.
- Must consider location of disease and machine limitations.

Treatment steps:

- Step 2: Neuroimaging.
Neuroimaging

- Requires at least two data sets to be “FUSED” into one.
  - CT with frame
    - Thin Cut 1.25 mm
    - Planning sequence
    - No contrast
  - MRI
    - Disease specific sequences
    - Thin Cut: 1.25 mm
    - Obtained 2 days prior to treatment

Treatment steps:
- Step 3: Treatment planning
Treatment Planning

- Definition of “target” volume
- Normal tissue definition
- Choice of Dose for target
- Dose allowable for normal structures
- Conformality of dose
- Treatment duration.
- Most time consuming portion
- Done generally ahead of time to minimize patient waiting.

Treatment steps:
- Step 3: Treatment planning

Treatment steps:
- Step 4: Treatment and dose delivery
Treatment Delivery

- The frame on the patient is attached to table.
- The table is then moved to position each lesion at the focal point of the radiation
- Treatment times are extremely variable
  - 15 minutes to 90 minutes (so far)
  - Increase as sources decay
- Monitored by Medical Physicist and Radiation Oncologist & Neurosurgeon
- Patient discharged home
- Entire procedure generally about 4 hours or less.

Indications:

- Brain tumors: 80 %
  - Meningiomas
  - Vestibular Schwannomas
  - Pituitary tumors
  - Metastatic tumors - Most Common Indication
  - Gliomas
- Arteriovenous / Cavernous Malformations: 12 %
- Functional Neurosurgery: 8 %
  - Trigeminal neuralgia
  - Essential tremor
  - Obsessive Compulsive Disorder.
  - Mesial temporal lobe epilepsy

Brain Metastasis

- Single largest indication for GK.
  - ~ 250,000 cases yearly
- Use of Stereotactic Therapy growing
  - Increasingly effective systemic therapy
- Role of Whole Brain declining
  - More long term survivors
- Decision making very complicated
  - Prognosis, Disease status.
  - Disease, KPS, Age.
  - Multidisciplinary team
Brain metastasis

Brain Metastasis Survivals after Radiosurgery

<table>
<thead>
<tr>
<th></th>
<th>Median Survival</th>
<th>Tumor Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung Cancer</td>
<td>10 months</td>
<td>85%</td>
</tr>
<tr>
<td>Melanoma</td>
<td>7 months</td>
<td>90%</td>
</tr>
<tr>
<td>Renal Cell</td>
<td>11 months</td>
<td>90%</td>
</tr>
<tr>
<td>Breast</td>
<td>11-15 months</td>
<td>86%</td>
</tr>
</tbody>
</table>

Intracranial Meningiomas

- The optimal management of medically eligible patients is complete tumor resection.
- Impossible to achieve for most skull base tumors and tumors near venous sinuses
- Higher risk for the elderly or those with co-morbidities
- Many patients prefer a less invasive option

Intracranial Meningiomas

- Radiosurgery is not for:
  - Large meningiomas
  - Patients with symptomatic mass effect
  - Tumors in close proximity to the optic nerve with preserved vision
Intracranial Meningiomas

For skull base meningiomas, often GKRS is the optimal management because it leads to:
- Long-term tumor growth prevention or tumor regression
- Low risk of new neurological symptoms or signs
- Rapid return to current activity

Pituitary tumors

- Recurrent tumors after prior surgery
- Residual endocrine active tumors
- Patients without progressive optic neuropathy related to tumor compression of the optic apparatus
- Selected elderly or medically complex patients unsuitable for primary microsurgery or endoscopic surgery

Pituitary tumors

- The most common late complication of Gamma knife radiosurgery is the new onset of a pituitary hormonal axis deficiency (24%).
- The rate of pituitary insufficiency after GKS is lower than after conventional fractionated radiotherapy.
Vestibular Schwannoma

**Surgery V/S GKRS**
- In a comparison of 110 VSs resected surgically and 97 treated by SRS, a lower rate of facial palsy and a higher probability of preservation of functional hearing were both achieved after SRS.


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Trigeminal neuralgia

**Surgical Options for Trigeminal Neuralgia**

<table>
<thead>
<tr>
<th>Option</th>
<th>Invasiveness/Morbidity</th>
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</thead>
<tbody>
<tr>
<td>Microvascular decompression</td>
<td>most</td>
</tr>
<tr>
<td>Radiofrequency rhizotomy</td>
<td>least</td>
</tr>
<tr>
<td>Balloon compression</td>
<td></td>
</tr>
<tr>
<td>Glycerol rhizotomy</td>
<td></td>
</tr>
<tr>
<td>Peripheral nerve ablation</td>
<td></td>
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<tr>
<td>Stereotactic radiosurgery</td>
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</tbody>
</table>

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Trigeminal neuralgia

- Kondziolka and coauthors reported in their multi-institutional studies that initial improvement in trigeminal neuralgia was noted in 86% of patients.
  - 60% had complete pain relief without medications.
  - 17% had good pain response.
  - 8% showed slight improvement.
  - 14% had no improvement.

Trigeminal neuralgia

- The maximum level of pain relief is typically achieved within 1 month after radiosurgery.
- Complete pain relief within 1 week of treatment is reported in over 40% of eventual responders.
- More than three quarters of partial and complete responders will have responded within 3 months of treatment and
- More than 90% of responders by 6 months

Conclusions

- GKRS is a very accurate, minimally invasive modality of treatment.
- It is indicated for treatment of multiple intracranial pathologies.
- Indications are varied and diverse.
- It can be used as an adjunct to surgery or as a primary modality of treatment.

Questions???