THE GOLD STANDARD IN INTRACRANIAL RADIOSURGERY

LEKSELL GAMMA KNIFE® ICON
GIVING SOUTH AFRICANS LOCAL ACCESS TO THE GOLD STANDARD FOR THE TREATMENT OF BRAIN CONDITIONS

Exclusively for the brain: Gamma Knife Icon is the only non-invasive radiosurgery system specifically engineered to only treat delicate brain tissue.

It is the most proven radiosurgery treatment (documented outcomes).

This is the only Gamma Knife Icon machine in South Africa and in Africa, located at Netcare Milpark, Johannesburg.

MICROSCOPIC ACCURACY
Multiple beams deliver the exact prescribed dose to the target areas while sparing surrounding healthy brain tissue.

A GENTLE CARE EXPERIENCE
NON-INVASIVE TREATMENT
Gamma Knife is surgery without the scalpel.

NO HOSPITAL STAY
In typically a single outpatient session, patients receive a treatment plan and treatment. Treatment is completed in a few hours, with little to no side effects.
Intracranial SRS enables us to treat functional and vascular abnormalities and (traditionally) small brain tumors with surgical precision, but without the risks and potential side effects of open surgery in a highly sensitive area.

In SRS, radiation beams are focused precisely to the treatment target in order to damage cell DNA. Destroying cells’ ability to reproduce causes tumors to shrink over time – the effects are typically realized over weeks or months.

Due to the precise nature of SRS, higher more effective doses can be delivered in fewer treatments than traditional radiation approaches – all while sparing surrounding healthy tissue and nearby important structures.

- Non surgical treatment of functional and vascular abnormalities and small brain tumors
- Radiation beams are highly focused precisely to treatment target
- Radiation damages DNA of targeted cells
- Causes tumors to shrink, blood vessels to close off over time following treatment
- Enables fewer high dose treatments than other radiation treatment approaches
- Allows delivery of more effective dose while sparing collateral tissue / critical structures

**SRS GROWTH**

As illustrated by this chart, SRS for brain and CNS cancer is expected to grow dramatically over the next decade, opening new treatment possibilities for patients.

**INPATIENT AND OUTPATIENT SERVICES FOR BRAIN / CNS CANCER (US projected growth 2013-2023)**

<table>
<thead>
<tr>
<th>Service</th>
<th>Growth Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>SRS</td>
<td>71%</td>
</tr>
<tr>
<td>ED VISITS</td>
<td>19%</td>
</tr>
<tr>
<td>OTHER RADIATION THERAPY</td>
<td>16%</td>
</tr>
<tr>
<td>SURGICAL</td>
<td>15%</td>
</tr>
<tr>
<td>IMAGING &amp; DIAGNOSIS</td>
<td>14%</td>
</tr>
<tr>
<td>E&amp;M VISITS</td>
<td>13%</td>
</tr>
<tr>
<td>CHEMOTHERAPY</td>
<td>12%</td>
</tr>
<tr>
<td>HOSPICE</td>
<td>12%</td>
</tr>
</tbody>
</table>

**SRS SHOWING HIGHEST GROWTH RATE AMONG BRAIN CANCER THERAPIES**
The growth of SRS for brain metastases is supported by an increasing body of evidence and guidelines, such as:

- AANS/CNS guidelines
- NCCN guidelines
- ESMO guidelines (Breast, NSCLC)
- ASTRO guidelines
- DEGRO working group

**COST AND QUALITY OF LIFE CONSIDERATIONS**

**WHY SRS**

The question has shifted from whether or not SRS is a viable approach to treating brain metastases, but how to deliver it most effectively and efficiently to an expanded patient base. **For brain metastases, the question is not if SRS, but how it should be done.**

- SRS is proven and accepted for brain metastases
- Improved treatment of primary cancer – life expectancy
- Diagnosis of multiple mets increasingly common
- Quality of life more relevant
- Increased concern about neurocognitive issues
- Continued focus on cost effectiveness

**SRS FOR FUNCTIONAL DISEASE  PRECISION IS KEY**

Large patient populations incidence per million (% potentially treatable w/ SRS)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Incidence</th>
<th>Treatment with SRS</th>
<th>Science building support of SRS use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trigeminal Neuralgia</td>
<td>126-289</td>
<td>(50%)</td>
<td></td>
</tr>
<tr>
<td>Essential Tremor</td>
<td>237</td>
<td>(50%)</td>
<td></td>
</tr>
<tr>
<td>Epilepsy</td>
<td>450</td>
<td>(5%)</td>
<td></td>
</tr>
<tr>
<td>Behavioral Disorders</td>
<td>160-2,000</td>
<td>(2%)</td>
<td></td>
</tr>
</tbody>
</table>

Source: Incidence data and patients treated statistics 2009-2013 from Leksell Gamma Knife Society
Icon is the latest generation of Gamma Knife technology. Gamma Knife established SRS over 40 years ago, and continues to be considered the Gold Standard in radiosurgery with more than 1 million patients treated. What sets Gamma Knife apart is its exceptional precision and accuracy. **Gamma Knife established SRS >40 years ago.**

- Treats critically located brain targets with highest precision and selectivity
- The delivery of a high dose of irradiation through the intact skull
- Over 1,000,000 patients treated
- Gold Standard in radiosurgery

**PREFERRED TREATMENT FOR BRAIN METASTASES**

Preferred for the treatment of brain metastases, Gamma Knife effectiveness is well documented in professional literature, evidencing a high rate of control with a low rate of complications.

- #1 indication for Gamma Knife radiosurgery
- 400,000 metastatic tumors treated
- Well documented in literature
- High control with low complications
- Exceptional for multiple brain metastases
- Highest precision and accuracy
- Least dose to healthy tissue

**GAMMA KNIFE DOSE DELIVERY PRINCIPLE IS UNIQUE**

**EXCEPTIONAL PRECISION AND ACCURACY**

Gamma Knife technology is fundamentally different from that of a linear accelerator (linac). A linac emits X-rays from a single source. A multileaf collimator shapes the beam and must be moved around the patient by means of a gantry to control the dose delivery. The many moving parts require maintenance and quality control.

With Gamma Knife, up to 192 radiation beams (generated from radioactive Cobalt) intersect at a focal point and build up dose through individual shots to enable very precise sculpturing around the shape of a tumor – think ShrinkWrap – in terms of conformality.

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1 Based on numbers obtained from leksell gamma knife society. 2 Lippitz b et al. Cancer treatment reviews 2014;40:48-5
Radiation beams precisely directed to 1 or several lesions
- Each beam has very little effect on tissue it passes through
- Target tissue receives concentrated dose of radiation where beams intersect

Shape, dose of radiation optimized
- Focus on exact point desired
- Collateral tissue/nearby critical structures preserved

More specifically, with Gamma Knife:
- Radiation is delivered simultaneously through 192 beams that converge with very high precision in a defined target in the brain.
- The dose fall off is very steep, which minimizes radiation to healthy tissue.
- Shifting isocenter with each shot, modulation of individual beams, and sharp penumbra due to circular collimators and lower energy, enable dose distribution that is highly conformal to target while keeping dose to healthy tissue extremely low.
- A fully integrated system with very few moving parts minimizes risk of inaccuracies.
- The output is very stable and well known.

This fundamentally different technology produces fundamentally different results.
- 192 non-coplanar simultaneous beams
- Shifting of isocenter with each shot
- Few moving parts
- Modulation of individual beams
- Steep dose fall off
- Stable and known output

The leading solution for intracranial radiosurgery
Real-time motion management supports precision and accuracy.
Gamma Knife is optimised for and dedicated to intracranial SRS. On top of unique Gamma Knife benefits Icon offers seamless integration and optimisation of unique features:

- Integrated stereotactic Cone Beam CT enables imaging at the time of treatment
- Online Adaptive DoseControl allows information-guided quality control, plan adaptation to current characteristics of the treatment target
- Frame-based or frameless immobilization enables unlimited clinical and workflow flexibility for individualized intracranial SRS approaches to expanded indications
- Integrated stereotactic CBCT imaging
- Online Adaptive DoseControl™
- Exceptional dose deposition
- Immobilisation options:
  - Frame-based or frameless with High Definition Motion Management

UNIQUE ICON FEATURES
OPTIMISED FOR AND DEDICATED TO INTRACRANIAL SRS

Icon’s frameless SRS solution incorporates a thermoplastic mask and a High Definition Motion Management system. The mask is custom-shaped to the patient and allowed to harden. For the treatment session it is secured in place to keep the patient’s head still. Sensors mounted on either side of the patient’s head and adhered to the tip of the patient’s nose provide real-time tracking at the rate of 20 times per second. Motion deviation parameters can be set as low as 0.15mm. Should the patient move beyond the established parameters, the beam automatically shuts off. As the tracking system is infrared-based, it causes no additional dose to the patient.

- Real-time tracking: 20 times/sec
- High-definition: 0.15mm vs. 1mm standard
- Mounted on rigid device close to patient
- Beam off when patient motion is outside limits
- IR-based – no additional dose to patient

Similar level of accuracy frameless or frame-based

1 Based on numbers obtained from leksell gamma knife society. 2 Lippitz b et al. Cancer treatment reviews 2014;40:48-5
CONDITIONS THAT ARE TREATED

- Brain metastases
- Recurrent gliomas
- Benign tumours (e.g. meningioma)
- Acoustic neuromas/vestibular schwannomas
- Post-surgical pituitary tumours
- Vascular malformations (AVM)
- Trigeminal neuralgia
- Medication-refractory essential tremor

ADVANTAGES

- Highest dose delivery for precise targeting
- Guaranteed sub millimeter system accuracy
- Frame-based or Frameless treatment approaches
- Single or fractionated approaches
- Continuous quality control
- Streamlined workflow

TISSUE SPARING FOR THE BRAIN IS INCREASED 2–4 TIMES

Gamma Knife Icon offers multiple ‘modes of operation’ which allows optimal treatment for each patient based on their specific clinical needs.

**ICON SHOWS HIGHEST LOCALISATION ACCURACY VS. LINAC TECHNOLOGY**

**GAMMA KNIFE ICON**
- End-to-end locational accuracy 0.2mm for single and multi-targets target treatment
- Target movement during treatment 0.43mm, with HDMM limit set to 1mm
- Resolution of HDMM system 0.15mm

**LINAC**
- End-to-end locational accuracy 0.9mm for single target treatment and 1.2mm for single isocenter multi-targets treatment
- Target movement during treatment >1mm
- Resolution of IFMM system >1mm

**WORKFLOWS FOR FRAME-BASED OR FRAMELESS TREATMENT OPTIONS**

1. **G-FRAME OR MASK**
   - A: MRI
   - Plan: Non-stereotactic MRI
   - Immobilise
   - CBCT scan: Stereotactic ref & Patient Positioning
   - Online adaptation
   - TREAT
   - Dose Evaluation
   - Optional CBCT scan for additional QA

2. **G-FRAME**
   - Immobilise
   - MRI
   - Plan: Stereotactic MRI
   - Online adaptation
   - TREAT
   - Dose Evaluation
   - Optional CBCT scan for additional QA

6. Typical resolution standard competing infrared based systems.
EXAMPLES OF MICRORADIOSURGERY CASES

<table>
<thead>
<tr>
<th>BRAINSTEM AVM</th>
<th>PITUITARY ADENOMA</th>
<th>MULTIPLE METS</th>
<th>CAVEROUS SINUS MENINGIOMA</th>
</tr>
</thead>
<tbody>
<tr>
<td>45 YEAR OLD MALE</td>
<td>56 YEAR OLD MALE</td>
<td>63 YEAR OLD FEMALE</td>
<td>63 YEAR OLD FEMALE</td>
</tr>
<tr>
<td>No prior OP, Embol</td>
<td>Double vision</td>
<td>Breast cancer</td>
<td>No prior surgical resection</td>
</tr>
<tr>
<td>No hemorrhage</td>
<td>Prolactin level 1900</td>
<td>ER(+), PR(-), Her2/neu(+)</td>
<td>Lt. CN 4, 6 palsy</td>
</tr>
<tr>
<td>Facial pain</td>
<td>Bone and lung metastases (+)</td>
<td>No prior WBRT</td>
<td>Lt. facial numbness</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Bone and lung metastases (+)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>No prior WBRT</td>
</tr>
</tbody>
</table>

Images courtesy of University of Pittsburgh Medical Center, USA

POTENTIAL SIDE EFFECTS OF TREATMENT

Common side effects
- Headaches
- Local pain
- Local swelling
- Fatigue

Uncommon side effects
- Localized hair loss
- Localized tissue necrosis

Rare side effects
- Red and swollen skin
- Blistering and peeling skin
- Nausea and vomiting
- Visual Loss (depending on patient diagnosis and area of treatment)
- Hearing Loss (depending on patient diagnosis and area of treatment)
**LINEAR ACCELERATOR**

**TREATS MULTIPLE AREAS OF THE BODY**
Linear Accelerators are designed to address a diverse range of clinical needs throughout the body.

**EXTRA MARGIN COMMONLY ADDED SURROUNDING THE TARGET**
Extra margin or volume surrounding the target is commonly added to compensate for any possible shifts of the target.

**RADIATION SOURCE MOVES DURING TREATMENT**
Linear Accelerators rotate during the delivery of radiation. The source of radiation and the target are continually changing, introducing a source of potential error.

**HIGHER DOSE TO HEALTHY BRAIN**
During treatment to the brain, documented evidence reveals Linear Accelerator systems deliver two to three times more dose to normal brain and four to 100 times more dose to the body compared with Gamma Knife.

**MULTIPLE-DAY TREATMENT**
Treatment is typically delivered in 3 to 5 sessions over multiple days. (Multiple treatments are also referred to as fractionated delivery).

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**GAMMA KNIFE®**

**EXCLUSIVELY FOR THE BRAIN**
Gamma Knife’s fine-beam technology is specifically designed to treat delicate brain tissue.

**EXTRA MARGIN RARELY ADDED SURROUNDING THE TARGET**
Extra margin or additional volume surrounding the target is rarely added — sparing healthy brain tissue.

**RADIATION SOURCE REMAINS FIXED DURING TREATMENT**
With Gamma Knife there are no moving parts during the delivery of radiation. The source of radiation and the target are always in a fixed relationship during treatment, ensuring the highest degree of accuracy.

**LEAST DOSE TO HEALTHY BRAIN**
Documented evidence reveals that during treatment to the brain, Gamma Knife delivers two to three times lower dose to normal brain and four to 100 times lower dose to the body compared with other radiosurgery devices.

**TYPICALLY A ONE-DAY TREATMENT**
With Gamma Knife, treatment is typically delivered in a few hours on a single day.

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