

THE GOLD STANDARD IN INTRACRANIAL RADIOSURGERY



GAMMAKNIFE

SOUTH AFRICA

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).

There is only one Gamma Knife ICON machine in South Africa, and on the African continent, 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 STEREOTACTIC RADIOSURGERY (SRS)



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.

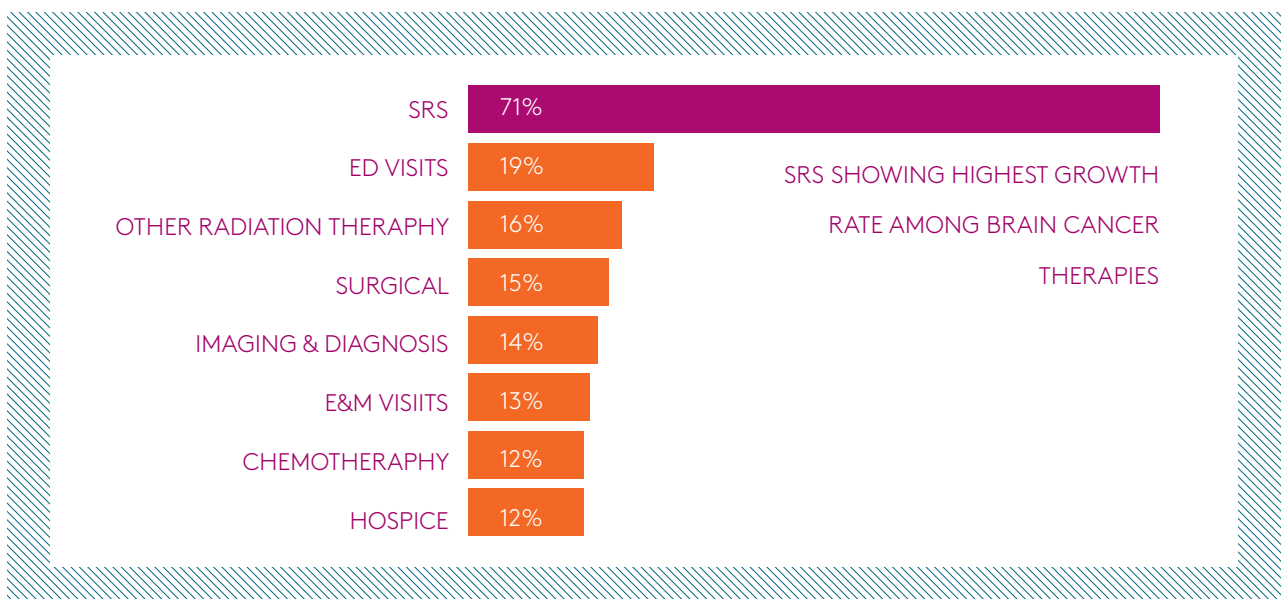
Due to the precise nature of SRS, higher more effective doses can be delivered in fewer treatments than traditional radiation approaches – all while sparing surrounding healthy tissue and nearby important structures.

- 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)



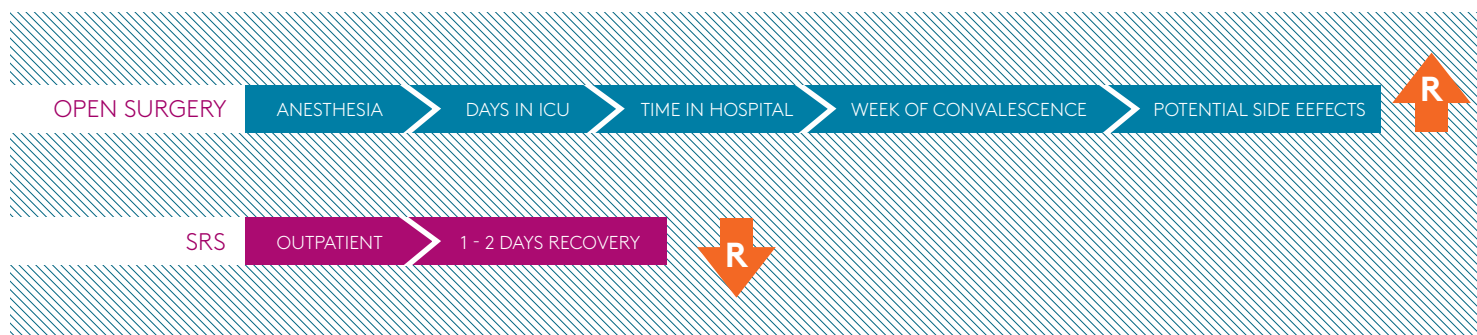


USE OF SRS FOR BRAIN METASTASES: INCREASING BODY OF EVIDENCE AND GUIDELINES

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

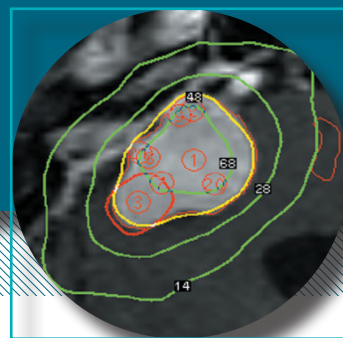
The question has shifted from whether or not SRS is a viable approach to treating brain metastases, but how to deliver it most effectively and efficiently to an expanded patient base. **For brain metastases, the question is not if SRS, but how it should be done.**

- SRS 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)

	Trigeminal Neuralgia	126-289	(50%)	Science building support of SRS use 	49.2% Growth of functional cases treated with Gamma Knife in the last five years
	Essential Tremor	237	(50%)		
	Epilepsy	450	(5%)		
	Behavioral Disorders	160-2,000	(2%)		



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 treated¹
- 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 treated¹
- Well documented in literature
- High control with low complications²
- Exceptional for multiple brain metastases
- Highest precision and accuracy
- Least dose to healthy tissue

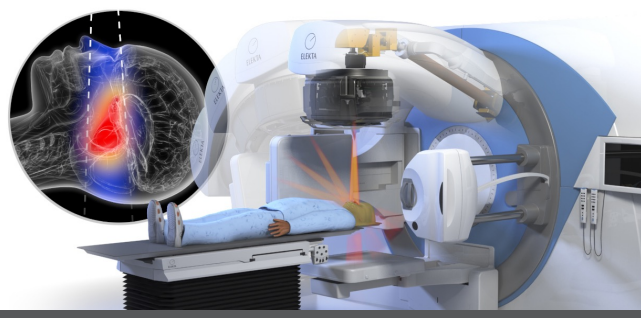


GAMMA KNIFE DOSE DELIVERY PRINCIPLE IS UNIQUE EXCEPTIONAL PRECISION AND ACCURACY

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 conformity.

LINEAR ACCELERATOR



GAMMA KNIFE ICON





Radiation beams precisely directed to 1 or several lesions

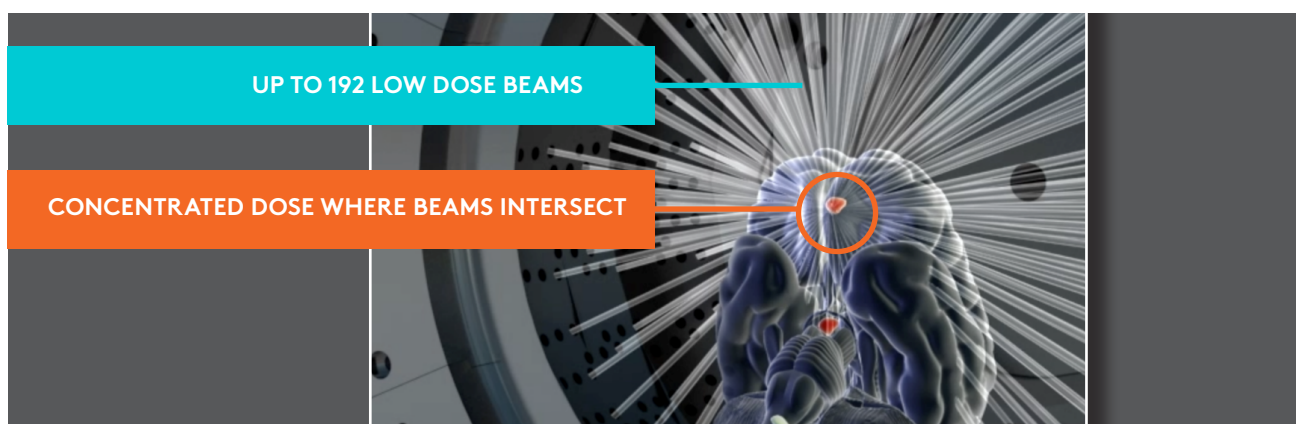
Each beam has very little effect on tissue it passes through

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



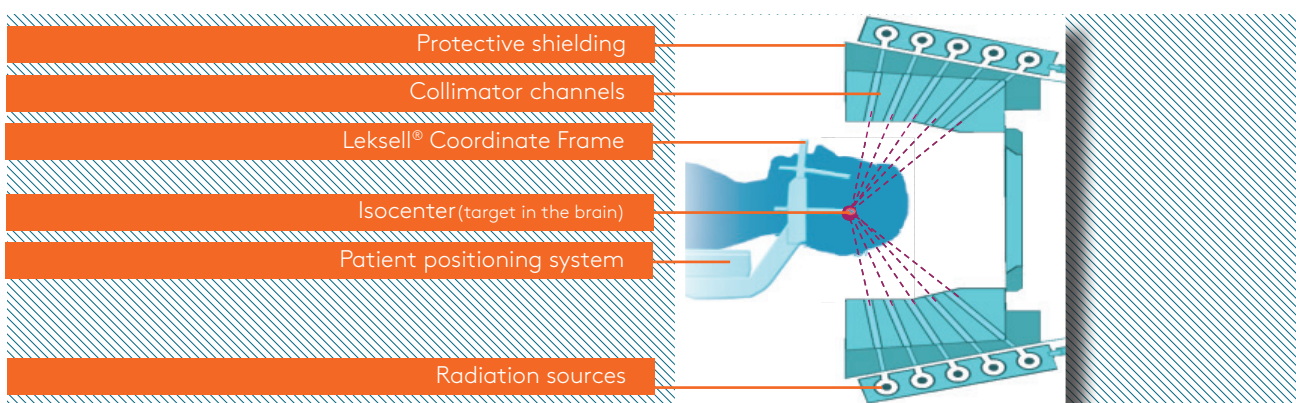
More specifically, with Gamma Knife:

- 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.
- And, the output is very stable and well known.
- This fundamentally different technology produces fundamentally different results.

This fundamentally different technology produces fundamentally different results.

- | | |
|--|----------------------------------|
| ■ 192 non-coplanar simultaneous beams | ■ Modulation of individual beams |
| ■ Shifting of isocenter with each shot | ■ Steep dose fall off |
| ■ Few moving parts | ■ Stable and known output |

The leading solution for intracranial radiosurgery





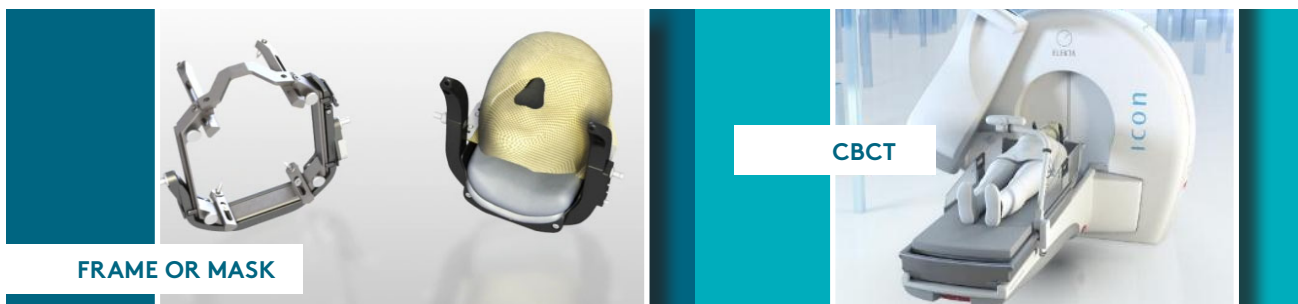
UNIQUE ICON FEATURES

OPTIMIZED FOR AND DEDICATED TO INTRACRANIAL SRS

Real-time motion management supports precision and accuracy.

Gamma Knife is optimized for and dedicated to intracranial SRS. On top of unique Gamma Knife benefits Icon offers seamless integration and optimization 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
- Immobilization options:
 - Frame-based or frameless with High Definition Motion Management



ICON FRAMELESS SRS SOLUTION

ENABLES THE MOST ACCURATE FRAMELESS TREATMENTS & ENHANCED PATIENT COMFORT

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



CONDITIONS THAT ARE TREATED

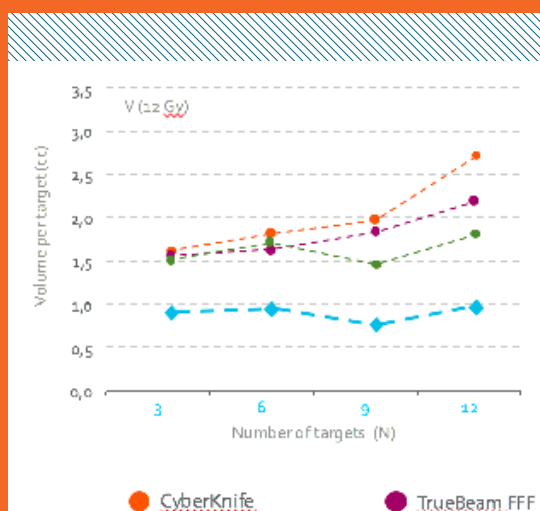
- Brain Metastases
- Recurrent gliomas
- Benign tumours (e.g. meningioma)
- Acoustic neuromas/vestibular schwannomas
- Post-surgical pituitary tumours
- Vascular malformations (AVM)
- Trigeminal neuralgia
- Medication-refractory essential tremour

ADVANTAGES

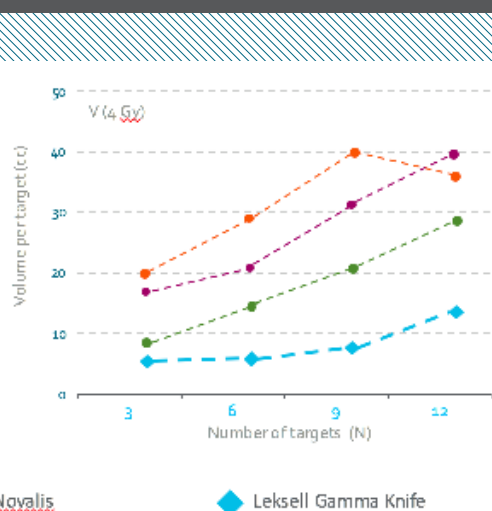
- Highest dose delivery for precise targeting
- Guaranteed sub millimeter system accuracy
- Frame-based or Frameless treatment approaches
- Single or fractionated approaches
- Continuous quality control
- Streamlined workflow

TISSUE SPARING FOR THE BRAIN IS INCREASED 2-4 TIMES

Volume of normal tissue receiving 12Gy
(predictor for necrosis)



Volume of normal tissue receiving 4Gy
(2.9Gy in hippocampus = cognitive decline)





ICON SHOWS HIGHEST LOCALIZATION ACCURACY VS. LINAC TECHNOLOGY

GAMMA KNIFE ICON

END-TO-END LOCALONAL ACCURACY 0.2MM FOR SINGLE AND MULTI-TARGETS TARGET TREATMENT¹
 TARGET MOVEMENT DURING TREATMENT 0.43MM, WITH HDMM LIMIT SET TO 1MM²
 RESOLUTION OF HDMM SYSTEM 0.15MM³

<0.5MM UNCERTAINTY



LINAC

END-TO-END LOCALONAL ACCURACY 0.9MM FOR SINGLE TARGET TREATMENT AND 1.2MM FOR SINGLE ISOCENTER MULTI-TARGETS TREATMENT⁴
 TARGET MOVEMENT DURING TREATMENT >1MM⁵
 RESOLUTION OF IFMM SYSTEM >1MM⁶

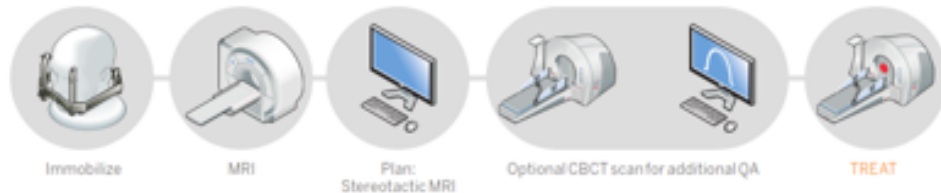
>1.5MM UNCERTAINTY

WORKFLOWS FOR FRAME-BASED OR FRAMELESS TREATMENT OPTIONS

G-FRAME OR MASK



G-FRAME



¹ Elekta (2015). Position accuracy analysis of the stereotactic reference defined by the CBCT on Leksell Gamma Knife® Icon™. Stockholm, Sweden: Elekta. ² Chung C, Liz W, Bootsma G, et al. Clinical evaluation of a novel thermoplastic mask system with intrafraction motion monitoring using IR tracking and cone-beam CT for Gamma Knife® radiosurgery. Poster session presented at ASTRO annual meeting; September 2014; San Francisco, CA. ³ Elekta (2015). High definition motion management - enabling stereotactic Gamma Knife® radiosurgery with non-rigid patient fixations. Stockholm, Sweden: Elekta. ⁴ Wen N, Li H, Song K, et al (2014). Evaluation of the systematic accuracy of cutting edge technology for stereotactic radiosurgery treatment. Poster session presented at ASTRO annual meeting; San Francisco, CA. ⁵ Boda-Heggeman J, Walter C., Rahn A., et.al. Repositioning accuracy of two different mask systems - 3D revisited: comparison using true 3D/3D matching with cone-beam CT. Int J of Rad Onc. 2006;66(5). Murphy, MJ. Intrafraction geometric uncertainties in frameless image guided radiosurgery. Int J of Rad Onc. 2009;73(5). Badakhshi H, Barelkowski T, Wust P, et al. Intrafraction variations in linac based image guided radiosurgery of intracranial lesions. Cancer Radiother. 2013;17, 664-687. ⁶ Typical resolution standard competing infrared based systems don't we need citation?

EXAMPLES OF MICRORADIOSURGERY CASES

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

Images courtesy of University of Pittsburgh Medical Center, USA

POTENTIAL SIDE EFFECTS OF TREATMENT

Common Side Effects

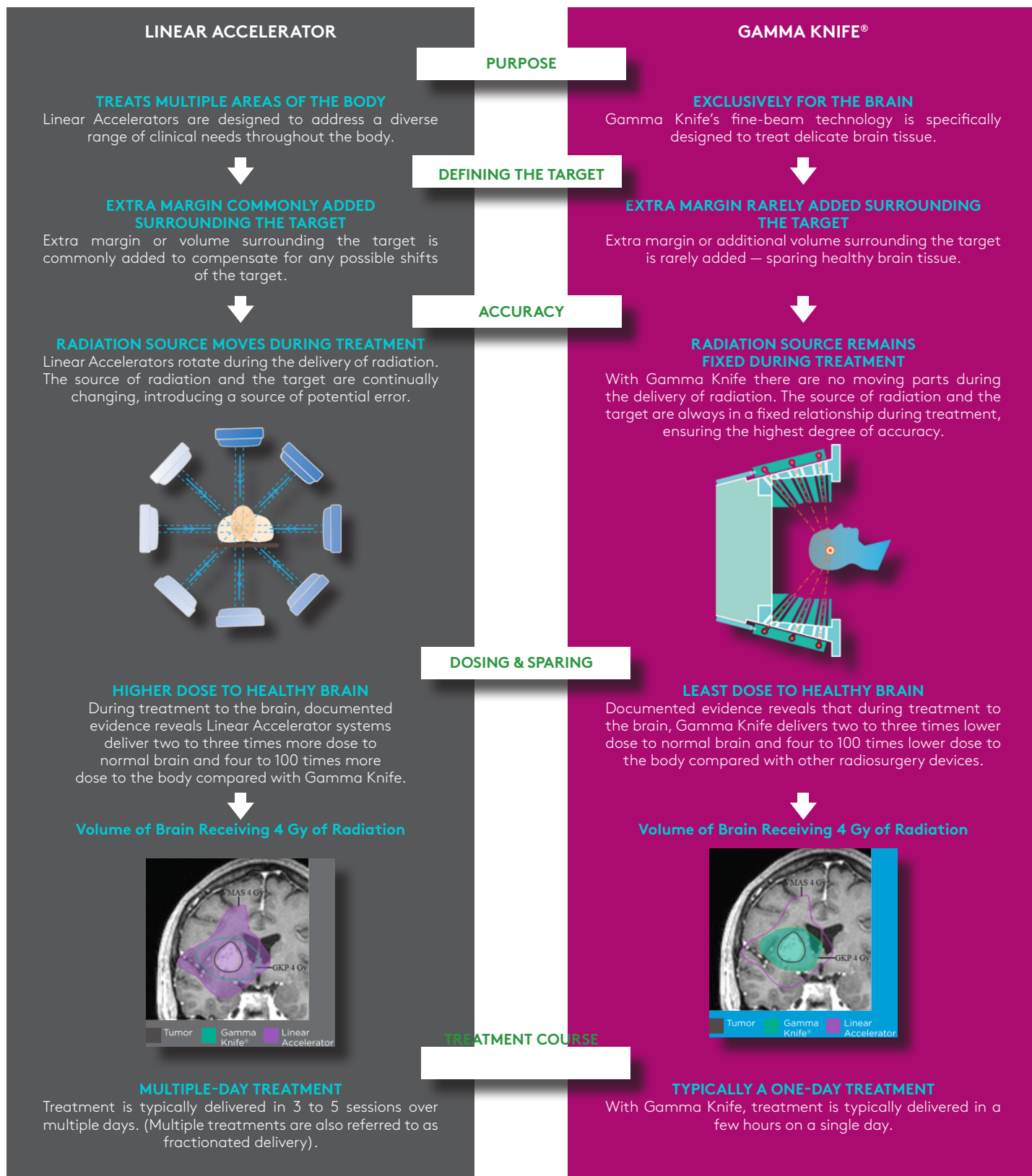
- Headaches
- Local pain
- Local swelling
- Fatigue

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)



Source: McDonald D, Sculer J, Takacs I, Peng J, Jenrette J, Vanek K. Comparison of radiation dose spillage from the Gamma Knife Perfexion with that from volumetric modulated arc radiosurgery during treatment of multiple brain metastases in a single fraction. J Neurosurg. 2014;121(Suppl 2):51-9



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