GAMMA KNIFE NEUROSURGERY – A REVIEW

Michael Torrens
Department of Gamma Knife Radiosurgery and Neurosurgery Clinic, Hygeia Hospital, Athens.

ABSTRACT

Gamma Knife radiosurgery has an established therapeutic role in neurosurgery with around 250,000 cases treated and a follow up over 20 years. The success and control rates have improved as more experience of appropriate dosage has been gained and as more planning accuracy has been achieved by new machines, new computer programs and better quality control. The currently quoted control rates for benign lesions less than 3cm diameter are: astrocytoma grade 1 – 92%, astrocytoma grade 2 – 87%, acoustic neuroma (vestibular schwannoma) – 96%, meningioma – 96 to 99%, non-secretory pituitary adenoma – 92%, GH and ACTH secreting adenomas – 80%, prolactin secreting adenomas – 40%, chordoma and chondrosarcoma – 73%, glomus tumour 100%, epilepsy (mesial temporal sclerosis) – 81%, trigeminal neuralgia – 83%, parkinsonian tremor 88%, parkinsonian rigidity/bradykinesia – 66%, obsessive compulsive neurosis – 60%, arterio-venous malformation 90%, cavernoma – 86%, uveal melanoma – 84%. In malignant glioblastoma, mean survival of 116 weeks has been described. In cerebral metastases the lesions can be controlled in almost every case so that survival then depends on the extracerebral disease. In many cases these various results have been achieved after failure of surgery or radiotherapy treatments. Complications are significantly less than with microsurgery, radiotherapy or LINAC based radiosurgery. The method is more cost effective than traditional surgical treatment and is also more acceptable for the patients.

INTRODUCTION

The Leksell Gamma Knife (fig. 1) is a well known treatment method, especially to neurosurgeons, but there exist some misconceptions which it is the intention of this paper to clarify as well as to review the contemporary indications for Gamma Knife treatment.

Gamma Knife is not a form of radiotherapy. Radiotherapy relies for its effect on the differential radiosensitivity of neoplastic tissue and the ability of normal tissue to repair itself. Gamma Knife treatment is a form of surgical ablation that competes with microsurgery by producing targeted cell death. This results in shrinkage of tumours (including ‘radioresistant’ ones),
control of hormonal and electrical dysfunction and thrombosis of dysplastic vessels, all without the risks of open surgery.

**Mechanism of action**

Radiation from 201 separate cobalt sources is finely collimated. The rays all meet at one point. The size of the point target is adjusted by changing collimator helmets. The guaranteed machine accuracy is better than 0.5mm. A stereotactic frame is attached to the patient and the lesion target is located, guided by MRI, CT, PET and DSA images that can be fused together. Multiple target isocentres are used to create a treatment plan in three dimensions that exactly fits the lesion shape with insignificant radiation to normal tissue. An even higher accuracy and selectivity has been achieved with the new model ‘C’ Gamma Knife by using many more small (4mm) isocentres combined with an automatic positioning system controlled by computer which rapidly changes the patient’s position between each treatment isocentre.

Because of the fine collimation of the rays, the accuracy of engineering and automatic positioning system, the absence of radiation source movement together with excellent calibration and quality assurance, the Gamma Knife ‘C’ is by far the most accurate and selective radiosurgery machine as yet developed. For this reason it is not always appropriate to quote results from older reviews using the ‘B’ model or other systems.

**Gamma Knife versus LINAC**

All machines giving a similar defined radiation dose to a target should have the same effect at the target. Those who claim that a LINAC systems are just as effective as a Gamma Knife are correct. The problem is that the LINAC is also effective on the surrounding tissues outside the target, causing a higher risk of complications due to its lower selectivity (fig 2). This risk, the normal tissue complication probability (NTCP) has been shown to be 2-4 times higher using a LINAC (1). While surrounding damage may not matter much in a frontal lobe metastasis, it matters a great deal elsewhere.
Consequently they have less experience. This, combined with a less accurate machine, produces not only more complications but also worse tumour control. Shaw et al. (2) have documented a 2.84 times greater risk of local tumour progression after LINAC treatment as compared with Gamma Knife.

As noted above, the guaranteed accuracy of isocentre location is to within 0.5mm for the Gamma Knife. In reality it is better than this, usually 0.3mm. The equivalent quoted accuracy of LINAC is 2.0mm. In reality it is often worse than this and deteriorates over time due to wear in the rotation bearings as the machine gets older.

In consequence most established LINAC units are resorting to stereotactic fractionated radiotherapy (SRT) to try to reduce the complication rate. This has the potential disadvantage of a lower long-term control rate in benign lesions as well as being a longer and more complex therapy.

**Fractionation**

The definition of radiosurgery, from the first use of the word by Lars Leksell in 1951, has always been a single dose therapy. Fractionation in time is therefore not radiosurgery but radiotherapy. The Gamma Knife has been criticized as being unable to deliver stereotactic fractionated radiotherapy in situations where it may be appropriate such as malignant lesions in the brain stem. In fact it is exactly the same in practice as SRT using LINAC. Treatment using both systems can be repeated as often as required as long as the patient can tolerate the frame on the head, certainly several days.

There is another form of fractionation that is really multiple single doses – fractionation in space. Where a lesion is larger than 3-3.5cm in diameter and the risk of complications becomes greater, then treatment can be given to two or more areas at intervals ranging from one day to several months. This is especially appropriate for AVM’s.

**Conditions treatable**

The various diseases and disorders that have been effectively treated by Gamma Knife radiosurgery are listed in Table 1 and the frequency of occurrence shown diagrammatically in pie charts in Figure 3. The source of information is the Leksell Gamma Knife Society, which monitors Gamma Knife activity and performance all over the world.

Figure 3

![Pie chart showing conditions treatable by Gamma Knife radiosurgery](image)
PRIMARY BRAIN TUMOURS

Low grade astrocytomas

Total resection of grade 1 and 2 gliomas is usually dangerous or impossible, even though advanced imaging techniques often reveal a well-defined tumour margin. For lesions that cannot be controlled by surgery (fig. 4), Gamma Knife has been used with good effect. We have personal experience of a number of children with recurrent, and therefore growing, pilocytic astrocytomas all of whom have been controlled by radiosurgery. In a recent series (3) the control rate in grade 1 was 91.7% and in grade 2 was 87.2%.

High grade astrocytomas

Survival in patients with malignant glioma increases as the dose of radiation increases but the dose is limited by the risk of radionecrosis of surrounding brain. Supplementary local boost radiation using brachytherapy has been used with good effect (4) but the open stereotactic procedure has a risk of about 1% for each target. However one of the best median survival rates in glioblastoma (110 weeks) was recorded in cases treated by thermo-brachytherapy (5).

Gamma Knife radiosurgery can be delivered with better conformity than brachytherapy and without the risks of implantation. A review of this technique has reported median survival in glioblastoma (RTOG grade 3) of 116 weeks (6). It may be possible to improve on this figure by using PET to target the active tumour. L-methyl (11C) methionine PET has been shown to correlate better to active tumour than CT or MRI enhancement (7) and we hope to report on the value of this targeting method soon. As is well known, survival is strongly related to RTOG grading but it seems that poor prognosis patients (RTOG grades III-V) have more to gain than RTOG grades I-II (6).

Haemangioblastoma

Haemangioblastoma is relatively easy to excise when single and associated with a cyst. When multiple (von Hippel Lindau disease), excision is often impossible. In such cases Gamma Knife has been used and the result, in small series, has been control in almost every case.

Figure 4. Pineal region astrocytoma before and after radiosurgery
Up to 50% of all patients with malignancies will develop brain metastases and, after radiotherapy alone, more than half of these will die from progressive neurological disease. In the past, surgical excision of accessible metastatic tumours combined with whole brain radiotherapy (WBRT) was thought to be the treatment of choice for single metastases. Several studies, however, have shown that Gamma Knife treatment of single metastases (fig. 5) can produce tumour control and survival as good as surgery plus WBRT (8). Moreover the results for Gamma Knife are the same for multiple metastases as for a single lesion (9), the chance of local recurrence is less than after surgical removal and control does not depend on the histological diagnosis. Since radiosurgery is more cost effective, easier for the patient and has a much lower complication rate, it would seem that the only indications for surgery are rapid neurological deterioration due to mass effect and the large (>3.5cm) diameter single lesion especially in the posterior fossa where any temporary oedema due to radiation would have serious results. The remaining indications for WBRT are multiple tumours (>10-15) or miliary lesions and CSF seeding.

Gamma Knife treatment can control >90% of metastatic brain tumours and complications, usually transient swelling after about 9 months which is controllable by steroids, occur in 5-10% (10). 80% 3 year survival has been achieved in cases where the extracranial disease has been controlled (11).

In a comparison of Gamma Knife treatment with WBRT the quantity and quality of survival was better with Gamma Knife (12). It is not clear how much benefit WBRT has in preventing new metastases since these may develop by new spread after treatment has finished. Accordingly the present recommendation is to repeat Gamma Knife surgery as necessary and avoid all WBRT. In this way patients will not die from the brain metastases and prognosis depends only on the extracranial disease.
ACOUSTIC AND OTHER NEUROMAS

Due to great improvements in surgical technique and the introduction of cranial nerve monitoring, microsurgeons have reduced the mortality and morbidity of acoustic neuroma surgery. Samii (13) has reported 97% tumour control with 93% normal facial movement (Grade I-II) and 47% hearing preservation. At the time of publication (1997) this was equal to the results from the ‘B’ series Gamma Knife (90% facial function and 50% hearing preservation). However, unfortunately, not all patients can be operated by a Samii. Average results, including those from the American Acoustic Neuroma Registry, are 90% tumour control (10% recurrence or death), 80% adequate facial nerve function and 6-30% hearing preservation (14,15). In addition there is 1% or more mortality even in centers of excellence (14).

At the same time the results from using highly conformal and selective, multiple isodose Gamma knife treatment with the ‘C’ series machine have improved. The results reported contemporaneously (16,17), using a marginal dose of 12Gy, are of 100% normal facial function and 59-70% hearing preservation (fig. 7) together with 96% control of tumour growth.

Except for having 0% mortality, the Gamma Knife treatment also has a much lower incidence than microsurgery of the minor complications and disabilities that are usually not discussed but are common after open operation (18). For example, minor neurological or functional deterioration (GK 9%, microsurgery 39%), hospital stay (GK 3 days, microsurgery 23 days), time away from work (GK 7 days, microsurgery 130 days), proportion keeping the same job (GK 100%, microsurgery 56%) (17).

It is clear that, for smaller acoustic neuromas, Gamma Knife surgery (fig. 6) is the treatment of choice. For larger lesions (>3cm) fractionation in space may be chosen, especially in the elderly, or subtotal removal followed by interval radiosurgery for the remnants, which is safer than attempts at total removal in all but the most experienced surgical hands.

The same comments apply in principle to all other intracranial neuromas.
MENINGIOMAS

Figure 7. The percentage risk of cranial neuropathy following Gamma Knife depends on the size of the acoustic neuroma but in all cases is significantly less than the risk after microsurgery.

Figure 8. Illustration of the dose plan for an infiltrating meningioma of the cavernous sinus showing conformal treatment (yellow line) and that even low doses (10Gy green line) can be designed to avoid the optic chiasm (blue line).

The mortality and morbidity of total surgical removal of meningiomas of the skull base and venous sinuses is still unacceptably high. Many surgeons elect to perform a subtotal removal in which case recurrence during the patient’s lifetime is at least 55%.

Gamma Knife therapy (fig.8) has been shown to control 96-99% of meningiomas less than 3cm diameter, with two thirds of the tumours becoming smaller (19,20). Average morbidity (usually transient cranial nerve palsies) is 2%. This control is maintained over the long term. A ten year
follow up study, which would have used the inferior, less conformal techniques of the ‘U’ and ‘B’ series gamma knives, showed 93.1% tumour control (21).

It is no longer acceptable to damage the patient by attempting complete removal of meningiomas. Elective surgical policy should be primary gamma knife treatment of tumours less than 3cm diameter (except those on the convexity dural surface) and partial removal followed by Gamma Knife treatment for larger tumours. If the tumour is very close to the optic nerve then a cushion of fat, Teflon or other material should be inserted to create a space between the tumour and the nerve. This allows safer and more effective radiosurgery later (the same applies to pituitary tumours). During a recent EANS debate (22) the notable experts Al Mefty, Samii and Dolenc all agreed with this strategy. Al Mefty suggested waiting until the residual tumour actually shows signs of growth since, as noted above, the tumour may remain dormant.

PITUITARY TUMOURS
Adenomas

![Figure 9. Pituitary adenoma before and 54 months after treatment](image)

Surgical removal of pituitary adenomas is, at present, the treatment of first choice because it is effective immediately. The new minimally invasive techniques, such as transnasal endoscopic or endoscopically assisted approaches, are better tolerated by the patient and complications should be minimal. However total removal of macroadenomas is almost impossible and hormonal control of functioning microadenomas by surgery is reported to be 23-77% (23). There is therefore a high incidence of failure or recurrence. Also some patients, especially those with Cushings disease have a high operative risk. Attempts at second operation are much more difficult and dangerous.

It follows that Gamma Knife treatment (fig. 9) is used most often when surgery has failed. Even in these cases normalization of hormone function can be achieved in 35-95% depending on diagnosis (23,24,26). Tumour growth control rate is 92%, shrinkage occurs in 65-80% (25). Non-secretory adenomas respond best. Among secretory microadenomas, growth hormone and ACTH secretion responds best (60-80%) with a lesser effect on prolactin (40%) (25).
Normalisation of growth hormone in 96% of cases at 2 years has recently been reported (26). Better results have been obtained in recent years since it was realized that treatment with bromocriptine and somatostatin protects against the effects of radiosurgery. Treatment with such drugs must be stopped before using the Gamma Knife. Radiosurgery has a continuing effect on hormonal control even beyond 4-5 years and long delayed success is now recognized. There is also a late incidence of hypopituitarism of up to 20% (25). For these reasons, patients need lifetime follow up.

Comparison of Gamma Knife with conventional radiotherapy (27) shows that Gamma Knife works faster and more effectively with less risk of complications such as hypopituitarism or optic nerve damage. With more experience of dose calculation to achieve more curative and rapid effects without damage to functioning pituitary tissue, it is likely that Gamma Knife will replace surgery as primary treatment for microadenomas. Chiasmal compression will continue to require surgical intervention.

**Craniopharyngiomas**
Craniopharyngiomas continue to be a major surgical problem. The only hope for cure is total surgical removal at the first operation. Such surgery has a high mortality and morbidity, is only possible in about 10% of cases and the recurrence rate even after ‘total’ removal is 19% (28).

Conventional fractionated radiotherapy improves the ten year survival rates from 40% to 75% (29), but in children often causes impaired growth with mental and sexual impairment.

Use of the Gamma Knife alone has produced an 87% tumour control rate in 31 patients observed for 1-7 years (30), but larger groups and longer follow up are needed for evaluation of results. Gamma Knife has more often been used for recurrence after failure of conventional fractionated radiation. In these cases there is greater danger of radiation damage to the optic chiasm and to any residual pituitary function. It is better therefore to proceed straight to Gamma Knife and avoid radiotherapy.

Management of this condition is very complex. Radiosurgery often needs to be combined with stereotactic cyst aspiration and/or installation of Yttrium (31) or bleomycin (32). Such multimodality approach requires a team with experience of microsurgery, radiosurgery, stereotaxy and radiotherapy.

**OTHER SKULL BASE TUMOURS**
Tumours that infiltrate the skull base are often even more difficult to manage surgically than meningiomas. The spectrum includes chordoma, chondrosarcoma, glomus tumour, haemangiopericytoma, paranasal sinus carcinoma, juvenile angiofibroma, esthesioneuroblastoma and metastases.

En bloc excision is potentially curative and so must be considered where possible. The majority of cases require management in other ways however and Gamma Knife is one of the most effective.
Haemangiopericytoma responds very rapidly and usually disappears, however it has a tendency for late recurrence and patients must be followed. Chordoma and chondrosarcoma, although ‘radioresistant’, have been controlled in 73% of cases (33). Metastases respond as expected and described above. Glomus jugulare tumours, where surgical resection is usually complex with many complications and recurrence is common, seem to respond very well. 100% control with 64% improvement of symptoms has been reported (34). Other conditions have been the subject of case reports and small series. Treatment is worth considering but large series are not available yet to predict success.

FUNCTIONAL DISORDERS

Epilepsy

In the series of patients with AVM treated at Karolinska by Gamma Knife it was observed that 52 out of 59 cases with epilepsy were cured of their fits even though the AVM was not always completely obliterated. This led to the concept that radiosurgery may modify epileptogenic activity and attempts were made to ablate the epileptic focus in other patients where it could be defined.

The largest experience is in mesial temporal sclerosis. Regis et al (35) performed amygdalohippocampectomy with the Gamma Knife and after this 81% of patients were seizure free at 2 years or more follow up. Ablation of the whole area of amygdala and hippocampus requires a large radiation dose and risks a local radiation reaction. Regis has concentrated recently on lesioning the parahippocampal gyrus, with satisfactory results and reduced complications. The results will be published shortly.

Research using magnetoencephalography, functional MRI and PET to localize epileptic activity is likely to increase the proportion of patients found to have focal epilepsy. These imaging methods allow stereotactic targeting of foci and the role of the Gamma Knife is likely to become more important.

Trigeminal Neuralgia

Figure 10. The lesion produced in the fifth nerve (left) and the 4mm collimator plan used to produce it (right).
A Gamma Knife lesion at the root entry zone of the fifth nerve (fig. 10) offers a high chance of improvement in drug resistant cases and avoids most of the morbidity of invasive surgical approaches. A multicentre study (36) showed 58% pain free, 36% improved and 6% unchanged. The risk of facial dysaesthesia is 2-4%. If the radiation dose is increased or repeated the cure rate is much higher but so is the risk of mild dysaesthesia. A recent study with a 90Gy dose gave a cure rate of 73% but a 16% incidence of dysaesthesia (37). Giving a second dose to failed cases resulted in an overall cure rate of 98% but all of those given a second dose suffered dysaesthesia (38). An even more recent study has identified the plexus triangularis, 5-8mm from the brain stem, as a more appropriate target with a cure rate of 83% and dysaesthesia 4% (39).

Post-herpetic trigeminal neuralgia, which does not respond to other surgical treatment (except brain stem DREZ lesions), has been shown to respond to the gamma knife in 44% of cases (40). Since the overall results of Gamma Knife radiosurgery can be better than other techniques it is likely to become progressively more popular.

**Parkinson’s disease and other dyskinesias**

There has been renewed interest in surgical intervention to treat Parkinson’s disease. This is due to the realization that many patients become refractory to levodopa after long-term use, combined with the occurrence of dyskinetic movements associated with Sinemet. The classical approach to stereotactic neurosurgery for Parkinson’s disease has been to perform lesions by placing an electrode in the appropriate target and heating it by radiofrequency current. The main complications are intracerebral haemorrhage and neurological damage due to misplaced lesions. The use of stereotactic deep brain stimulation has fewer cerebral complications but more practical problems associated with the implanted electrode and stimulator.

The Gamma Knife was originally designed and intended as an instrument for thalamotomy, but only recently have large series with adequate follow up been reported. In a series of 158 gamma thalamotomies for tremor the cure rate was 88% with results maintained at 4 years follow up (41). From the same center the relief of Sinemet induced dyskinesia by pallidotomy was 85% and pallidotomy also improved two thirds of patients with rigidity and bradykinesia. Two patients (1.3%) had a mild lesion induced neurological deficit.

The effectiveness of Gamma Knife treatment is the same as a traditional open stereotactic procedure but with much lower complications. The control of dyskinesia is delayed for 6-18 months from treatment.

**Chronic pain**

In general destructive lesions for the treatment of pain are to be discouraged, but it seems unreasonable to withhold the benefit of medial thalamotomy in cases of cancer pain where all else has failed. 65% of unilateral pain cases are effectively controlled in this way. Hypophysectomy is also useful in bone pain from Ca breast metastases. Both thalamotomy and anterior cingulotomy can benefit chronic pain of non-malignant aetiology but the indications and results are not yet clarified.
Obsessive-compulsive neurosis

An unscientific backlash against stereotactic psychosurgery has effectively halted operations in many countries but this is unjustified. In the subgroup of obsessive-compulsive anxiety it is well known that limbic lesions can rehabilitate socially destroyed patients. Many studies have shown that 60% of stereotactic anterior capsulotomy procedures are successful (42) and this is in agreement with my personal experience of 60 cases of subcaudate tractotomy and anterior cingulotomy performed in Bristol (43). It has been suggested that a single right-sided lesion may be adequate (42). The procedures are greatly underrated and a placebo controlled double blind study is currently underway in Sweden and USA using the Gamma Knife. The results should cause a change in medical and social prejudice.

VASCULAR CONDITIONS

Arteriovenous malformations

![Figure 10. A thalamic arteriovenous malformation before and two years after Gamma Knife treatment.](image)

There has been a very long experience of Gamma Knife treatment of AVM because accurate stereotactic localization was possible from angiography before the advent of CT and MRI. The first lesion was treated in 1972. This large experience has made it possible to develop computer programs to predict the results of treatment (44) and in particular the probability of total occlusion, the risk of radiation damage and the risk of haemorrhage before occlusion occurs. It is therefore possible for all units to calculate the dose that has the greatest chance of success and the lowest rate of complications.
Favourable factors for success of radiosurgery are lower flow, compact or plexiform lesions, multiple shunts or fistulas and few draining veins. Gamma Knife is particularly indicated when lesions are inaccessible to surgery and embolisation, or when a residual nidus remains after other treatment. It is also important to stress that the risk of radiosurgery is less than other methods and so it is appropriate as a primary treatment unless contraindicated, for example a single high flow fistula is best managed endovascularly.

Many groups have published similar results (44-46). Total obliteration in lesions less than 3cm diameter should be 40% at one year, 80% at 2 years and 90% at 3 years. Smaller lesions have a higher success rate and lower complication rate. The risk of local oedema due to radionecrosis is 2-4% and the risk of rebleeding within 2 years is also 2-4%. Associated epilepsy is usually abolished. Success and risk are strongly related to total dose and lesion size, rebleeding is inversely related to dose. For this reason smaller lesions, which can safely tolerate a higher dose, are more effectively treated.

The indications for microsurgery are certainly very limited now; mainly compact lesions at or near the convexity of the brain in non-eloquent areas. However it is not possible to say any one treatment is dominant. It is often necessary, especially in large lesions, to rely on multimodality treatment (46). In particular, embolisation followed after 3 months by Gamma Knife (to allow time for collaterals to open) has been a productive combination. It is evident that, for the best results, patients should be evaluated by a team experienced in microsurgery, embolisation and Gamma Knife surgery.

Cavernous angiomas (cavernomas)

Cavernomas are vascular malformations with well-defined margins and a surrounding haemosiderin deposit, but no angiographically demonstrable lesion. Often these are asymptomatic lesions that require no therapy. Recurrent bleeding or other symptoms may be cured by surgical excision if they are easily accessible but frequently they are not.

Two large series have established radiosurgery as the optimal therapy. Kondziolka et al. (48) reported 47 patients with bleeding cavernomas and noted a significant reduction in risk of bleeding from 32% per year to 9% per year. Kida et al. (49) analysed 51 cases presenting either as haemorrhage or intractable epilepsy. Haemorrhage was controlled in 86% and epilepsy was controlled in 64%. Permanent complications were 5%. The complication rate for radiosurgical treatment of cavernomas is unexpectedly high and this has been attributed to an amplification or radiosensitisation effect caused by the haemosiderin ring (50). For this reason doses should be less than for AVM of the same size and the haemosiderin ring should be excluded from the treatment plan.

ORBITAL LESIONS

Uveal melanoma

Enucleation of the eye does not prevent metastases and there has been a suggestion that it may encourage them. This has led to a search for treatments that conserve the eye and vision, control the tumour growth and preserve life. These include proton irradiation, Iodine-125 brachytherapy and Ruthenium plaque insertion all of which have practical problems and complications.
Gamma knife therapy has been used in certain centers with an ophthalmological interest for over 10 years. Initial high dose treatments were accompanied by severe side effects such as neovascular glaucoma (51). Reducing the dose has allowed the same rate of control (84%) and a reduced risk of glaucoma (16%). In another series there was 92% control (52). Over a 4 year follow up 13% developed metastases and 10% died of their disease.

Other orbital lesions

The feasibility of treating other conditions depends on the need to preserve vision by avoiding significant doses to the lens and optic nerve. Tumours such as haemangiomas, optic sheath meningiomas and optic nerve gliomas could be treated if the option of surgery is inappropriate. Recent experience in the management of very severe glaucoma has been encouraging with the pain being controlled in all cases and the mean intra-ocular pressure dropping from 40mmHg to 22.5mmHg (53).

COMPLICATIONS

It has been emphasized above in relation to particular lesions that the complication rate after Gamma Knife treatment is significantly less than after microneurosurgery, radiotherapy or LINAC based radiosurgery. However the Gamma Knife is a very powerful tool with potential complications and needs careful and experienced handling. The complications that exist are mainly minor and transient; they may be immediate or delayed.

Immediate side effects are moderate headache, skin hypersensitivity if the target is near the surface and acute cranial nerve disturbances (e.g. dizziness and vomiting after vestibular schwannoma treatment).

Delayed complications are mainly local swelling in or around the lesion 6-9 months after treatment (ARE – adverse radiation effect). This is dose related and can usually be controlled easily by steroids. The incidence is 2-10% depending on the target. Very occasionally radionecrosis occurs and may require decompressive surgery. This is usually because a larger than safely tolerated dose has been given in malignant disease and is therefore expected.

The complication that worries some observers is the possibility of radiation induced tumours. Because it is well known that radiotherapy can cause brain tumours it has been assumed that Gamma Knife can do the same. Radiotherapy for tinea capitis is well known to predispose to meningiomas (54) and fractionated radiotherapy for pituitary adenomas increases the risk of other local tumour formation by nine times compared with the normal population (55). There are reasons to believe that radiosurgery is less likely to induce tumours than radiotherapy but, up to now, there have been four cases in the over 200,000 patients treated by Gamma Knife (56). Because the delay to presentation may be as much as 30 years it is likely that this proportion will rise. However this miniscule risk, similar to frequent air travel, is unlikely to affect the indications for Gamma Knife treatment.

CONCLUSION

Assuming that the target is less than about 3.5 cm, it has been shown that the Gamma Knife can control a large proportion of the neurosurgical pathologies that occur in the brain. As in
every branch of medicine, correct selection of patients and judicious, quality assured, use of
equipment are of paramount importance.

In addition Gamma Knife is more economic than both LINAC radiosurgery and
microneurosurgery. The overall costs of Gamma Knife in a European environment (Austria)
are about 5% less than those of a dedicated LINAC (57). Gamma Knife is also significantly
more cost effective than microsurgery in both Europe and USA. For acoustic neuroma
treatment Gamma Knife costs less than half (41%) of surgical treatment (58). For the
management of metastases the cost is three quarters (74%) of surgical treatment (59).

Better control of malignant tumour growth is achieved using Gamma Knife. There is a 2.84
times greater chance of local progression of primary brain tumours and metastatic tumours
after LINAC radiosurgery as compared with Gamma Knife (2). For benign tumours the growth
control rate is similar in all radiosurgery treatments.

The most important advantage is that there are fewer complications than with microsurgery.
The treatment mortality is zero. No equivalent surgical operation can claim this. All studies
that have compared the incidence of more minor complications between Gamma Knife and
microsurgery have shown a huge reduction of complications by using Gamma Knife
radiosurgery (17,59).

There are also fewer complications than when using LINAC for radiosurgery. Because the
planning is more accurate, the risk is less when using the Gamma Knife, especially in areas
near the brain stem, skull base, cranial nerves and critical functional areas. Studies have
shown that the normal tissue complication probability (NTCP) is 2–4 times higher if a typical
LINAC is used (1). In practice the risk is even greater if the target is near the brain stem or
skull base.

Gamma Knife treatment has been subjected to a more intense and comprehensive follow up
than most contemporary treatment methods. Almost all of the results summarized above are
better than those of alternative treatments, despite the fact that the majority of cases were
managed using the earlier ‘U’ and ‘B’ models and with dose planning systems that were
primitive by today’s standards. When long term follow up of future series using the ‘C’ model,
the highly conformal ‘Leksell Gamma Plan’ and multi isodose treatment using the APS
(automatic positioning system) come to be analysed in a few years time, the results will
inevitably be even better.

References

1. Smith V, Verhey L, Serafo CF. Comparison of radiosurgery treatment modalities based on complication and
of recurrent previously irradiated primary brain tumours and metastases: Final report of RTOG protocol 90-95.


<table>
<thead>
<tr>
<th>TABLE 1. CONDITIONS TREATABLE BY GAMMA KNIFE RADIOSURGERY</th>
</tr>
</thead>
</table>

**PRIMARY BRAIN TUMOURS**
Low grade astrocytomas, high grade astrocytomas, haemangioblastomas, central neurocytoma, choroid plexus papilloma, germinoma, pineal tumours.

**METASTASES**

**NEUROMAS**
Acoustic, facial, trigeminal, jugular fossa.

**MENINGIOMAS**

**PITUITARY TUMOURS**
Non-secretory adenomas, hormone secreting adenomas, craniopharyngiomas, lymphocytic hypophysitis.

**OTHER SKULL BASE TUMOURS**
Chordoma, chondrosarcoma, glomus tumours, haemangiopericytoma, haemangioendothelioma, paranasal sinus carcinoma, juvenile angiofibroma, esthesioneuroblastoma, metastases.

**FUNCTIONAL DISORDERS**
Epilepsy, trigeminal neuralgia, Parkinson’s disease and other dyskinesias, chronic pain, obsessive compulsive neurosis.

**VASCULAR LESIONS**
Arteriovenous malformations, dural A-V fistula, cavernous angiomas.

**ORBITAL LESIONS**
Uveal melanoma, glaucoma, orbital haemangioma, optic sheath meningioma, optic nerve glioma, sub-foveal neovascularisation.