Gamma Knife® Surgery And Microsurgery: A comparison of published results

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INTRODUCTION

RADIOSURGERY, a term introduced by the Swedish neurosurgeon Lars Leksell, in 1951, refers to the destruction of a discrete target area in the brain using the precise delivery of a single, high dose of radiation through the intact skull. Subsequently the definition was modified to include in addition to destruction 'the production of a desired biological effect'. Early research efforts determined that cyclotrons (as a source for accelerated heavy charged particles) and linear accelerators (a source for variable energy photons) were then too cumbersome and complicated to perform radiosurgery. As a result, Leksell and biophysicist Dr. Borje Larsson designed the first Leksell Gamma Knife® as a dedicated neurosurgical instrument to deliver focused radiation for performing radiosurgery. Leksell Gamma Knife® consists of a hemispherical or doughnut shaped array of Cobalt 60 sources that naturally emit gamma ray photons at a predictable and easily quantifiable rate. These photons travel as high energy beams, several of which can be converged (focused) on a relatively small target volume. The 183 - 201 separate beams (depending on the model of the Leksell Gamma Knife® used) thus allow for a very precise delivery of radiation to the specified area while minimizing the radiation delivered to normal brain tissue adjacent to the target by distributing the incident radiation over a large volume. When used in conjunction with a stereotactic head frame, the precision of radiation delivery is 0.3 mm (0.01").

With the demonstration of the efficacy of Gamma Knife® Surgery considerable interest was evoked to adapt existing tools for radiation delivery for the purpose of radiosurgery. Such research,[1,2] was prompted primarily by cost considerations and led to the usage of a modified linear accelerator to perform radiosurgery, despite the recognized difficulties. Unlike the natural emission of gamma ray photons produced by Leksell Gamma Knife® cobalt 60 sources, a linear accelerator creates photons by accelerating electrons along a linear path where they collide with a metal target. The resultant single stream of photons must then be made to simulate multiple stationary beams by rotating the patient couch and by controlled movements of the accelerator gantry through multiple non-coplanar arcs around the patient's head.

As with any new technique the developers of radiosurgical techniques and pioneer users were cautious in applying it for different applications, however there now exists a large body of experience that establishes its efficacy and value in the modern management of numerous neurosurgical conditions. The outcomes and consequent cost-savings that can be achieved through radiosurgery have made this technique another tool in the neurosurgical armamentarium used to supplant and or replace conventional microsurgery as indicated in a given case. In this era of cost containment, this approach is of significant interest to third party payers, hospital associations, trade groups, and patient advocacy groups.

During the last several years, many comparisons have been made about the relative effectiveness of radiosurgery and microsurgery. Further, additional observations have been made about the relative effectiveness of modified linear accelerators in comparison to Gamma Knife® Surgery. However, organized long term follow up has been lacking. No objective outcomes-based data have been published. Nonetheless, it is extremely valuable to put into perspective the results currently available from the literature; such a synopsis may assist organizations in their evaluation of the role of available treatment modalities. This is the motivation for this compilation of data.

This is intended to serve not only as a ready reference for those who wish to quickly review the literature but also as a road map for those intending a deeper study. The diversity of the patient populations that are inherent in comparing two random series make the meta-analysis limited in scope. The caveat for those who see this data is that whereas Gamma Knife® Radiosurgery (GKRS) is a technique that is somewhat operator independent and therefore prone to produce more consistent results microsurgery remains an art that is mastered only with time and patience. The microsurgical results offered for comparison are therefore representing the state of the art and not to be equated with the average results of microsurgery. Whereas in a few indications Leksell Gamma Knife® emerges as the tool of first choice, in most others it remains as an equal contender and in some an adjunct to the microsurgery.

The data is compared by looking at different series of patients, without matching the treatment or patient parameters and without randomization or prospective observation. Nonetheless, this article represents the most comprehensive synopsis to date and is intended to facilitate comparison of the clinical effectiveness of the methodologies.

The principal observations are summarized as follows:

Gamma Knife® Surgery has established clinical efficacy for many currently reported indications. This includes obliteration rates in AVMs, and treatment success rates for acoustic neuromas, meningiomas and metastatic tumors. Gamma Knife® Surgery uniformly provides lower complication rates than microsurgery. Both mortality and morbidity rates are lower for radiosurgery. The more recent publications reporting results of Gamma Knife® Surgery in vestibular schwannomas (acoustic neuromas) indicate that it may actually emerge as the treatment of first choice as compared to the average results of microsurgery.

MATERIALS AND METHODS

MEDLINE® was used to search the world's clinical literature as of March, 2002, to obtain the current literature published on each of the diagnostic categories. The focus of the search was confined to patient series and review articles containing results from surgery, radiosurgery, radiation therapy and other forms of therapy. A preliminary list of abstracts was reviewed to eliminate those papers that did not have analyzable data. Data from the remaining papers were reviewed and compiled in summary tables. In this review the results reported from major centers of excellence have been emphasized.

The summary tables were derived from many authors' data which occasionally required re-analysis in a manner that differs from the original publication. When appropriate data were not cited or included in the article, the table indicates this with an appropriate notation either 'not applicable' (na) or 'not reported' (nr) and the cell is not included for purposes of averaging results. This approach acknowledges that surgeons practicing different modalities of treatment assess their results differently. It is also recognized that different authors using the same technique will assess their results differently. In calculating summary data we have used weighted averages, so that the impact of the results from any series in a group are proportional to the number of cases in the series. This minimizes the influence of small series with numbers that are at extremes of the data set on the overall summary figures.

RESULTS AND DISCUSSION

Arteriovenous Malformations

Arteriovenous malformations (AVMs) are comprised of abnormal blood vessels which provide unnatural connections or 'shunts' between arteries of the brain and its draining veins. This malformation bypasses the normal brain capillary system and therefore does not provide nutrition to the normal surrounding brain tissue. The abnormal construction of these blood vessels and the relatively high volume of the blood flowing through them leads to the risk of bleeding (hemorrhage), strokes, seizures, and progressive neurological deterioration for the patient.

Since the first descriptions of these lesions by ancient Egyptians in 1500 BC,[3] they have continued to be surrounded by controversy. Although there have been major advances in the diagnosis and treatment of these lesions, there is no consensus on a universal approach to their management. The available evidence,[4, 5 6-8] indicates, however, that left to themselves, as many as two thirds of all patients with AVMs will be symptomatic and at least half of these symptomatic patients will endure serious complications like bleeding. Currently the annual risk of a brain hemorrhage is estimated to be between 1 and 5% per year[9-11]; over a 25 year observation period more than 40% of patients with these congenital lesions will have a hemorrhage, with an annual risk of death of 1% per year. The development of new diagnostic modalities like MRI have resulted in the increased discovery of silent AVMs whose natural history has not yet been studied. Although there is general agreement that most AVMs that bleed must be treated, differences of opinion remain regarding the management of unruptured AVMs.

Microsurgery deals with AVMs by excision (removal) through a craniotomy (an opening in the skull). According to literature, complete removal of an AVM may require anywhere from 1 to 5 separate operations, depending on the location, size and pattern of deep venous drainage. The surgical approach to these lesions is well documented in the literature and several major series have been included in this analysis. A total of 2,722 patients were reported in various microsurgical series . The rates of complete resection are not always reported, nor are the number of procedures required in each case always documented. Complete resection figures have varied from 82% to 100% (Table 1). As a benchmark an average of the complete surgical obliteration (excision) rates for the various series were calculated to be 94.7% (Figure 1), using one or more craniotomies in order to accomplish the goal of complete obliteration. Morbidity rates vary from 1.4% to 44% (Mean 11.7%) and mortality rates vary from 0% to 13% (Mean 4.4%).[12-36] Average mortality rates over the decades show a downward trend. This downward trend is a reflection of the improvements in surgical technique and perioperative care. Nonetheless,

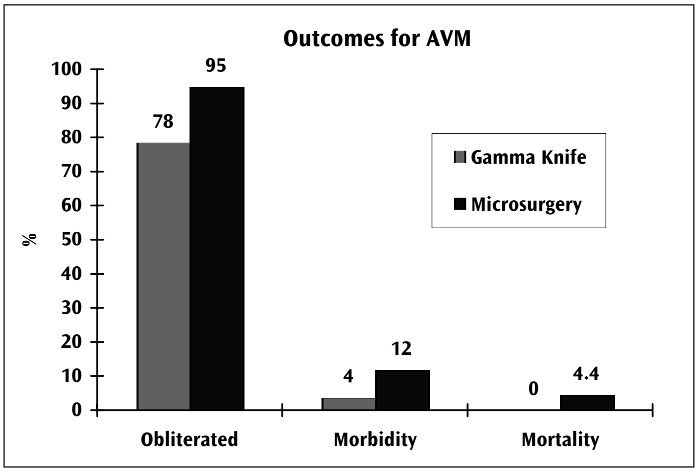

Figure 1. Outcomes for AVM management

these figures, when viewed in conjunction with the fact that there are lesions in locations which daunt even the boldest of surgeons, have prompted the quest for other treatment modalities. The best results from AVM microsurgery are reported from centers of excellence where experience and team approach are emphasized; such published results however may not reflect the actual results achieved at other neurosurgical centers, especially those with more modest experience.

Radiosurgery was used to treat AVMs for the first time in 1971, with Leksell Gamma Knife® as the tool. Radiosurgery works by inducing a slow occlusion of the malformation. This is due to a rapid proliferation of cells in the layers that comprise the blood vessel wall induced by the radiation. This results in progressive narrowing of the vessel lumen and a consequent slowing of flow. Ultimately thrombosis (formation of an occlusive blood clot) occurs in the malformation. After a single Leksell Gamma Knife® surgical procedure the process of obliteration can take from 6 months to 3 years. The average time to occlusion is two years (at which point 80% to 90% of AVMs will be completely obliterated).

TABLE 1. OUTCOME FOR ARTERIOVENOUS MALFORMATIONS

Treatment modality	*Year*	*No: Cases*	*% Obliterated*	*%Morbidity*	*Surgical Mortality*	*% Rebleed*	*%Rebleed Mortality*
Leksell Gamma Knife®							
Chang[42]	2000	277	79	5.0	0.0	6.8	nr
Regis[329]	2001	45	82	4.5	0.0	0.0	0.0
Kurita[43]	2000	30	70	0.0	0.0	16.0	12.0
Massager[44]	2000	87	72	4.6	0.0	4.0	1.4
Coffey[41]	1995	121	72	2.5	0.0	4.0	2.0
Pollock[40]	1995	65	91	1.5	0.0	7.7	3.1
Steiner[37]	1994	880	80	3.1	0.0	2.3	0.9
Kondziolka[39]	1993	402	71	3.1	0.0	5.2	1.7
Sutcliffe[38]	1992	160	76	3.8	0.0	3.8	0.6
Summary Data		**2067**	**78.4**	**3.6**	**0.0**	**4.3**	**1.1**
Microsurgery							
Pikus[14]	1998	72	97	8.3	0.0	na	na
de Oliveira[12]	1997	18	83	16.6	5.5	na	na
Kikuchi[13]	1997	9	89	44.0	0.0	na	na
Deruty[18]	1993	40	93	27.6	6.7	na	na
Grzyska[17]	1993	76	82	17.1	2.6	na	na
Morgan[19]	1993	112	nr	18.0	3.6	na	na
Pipegras[20]	1993	267	98	nr	4.5	na	na
Sisti[15]	1993	67	99	1.4	0.0	na	na
Yeh[21]	1993	54	100	14.8	0.0	na	na
Heros[22]	1990	153	90	7.8	0.6	na	na
Steinmeier[23]	1989	48	nr	10.0	0.0	na	na
Yasargil[24]	1988	414	94	12.8	2.4	na	na
Spetzler[16]	1986	45	98	2.2	0.0	na	na
Davis[25]	1985	69	nr	8.7	1.5	na	na
Lussenhop[26]	1984	90	97	11.0	2.0	na	na
Stein[27]	1984	180	97	15.0	1.1	na	na
Albert[28]	1982	124	nr	nr	12.0	na	na
Pertuiset[29]	1982	162	nr	nr	11.0	na	na
Guidetti[30]	1980	98	97	6.3	6.3	na	na
Parkinson[31]	1980	90	nr	20.0	4.4	na	na
Drake[32]	1979	140	nr	11.0	11.0	na	na
Nornes[33]	1979	63	92	3.0	1.6	na	na
Pelletteieri[34]	1979	119	94	8.4	13.0	na	na
Suzuki[35]	1979	147	nr	3.0	3.0	na	na
Wilson[36]	1979	65	nr	28.0	6.0	na	na
Summary Data		**2722**	**94.7**	**11.7**	**4.4**	**na**	**na**

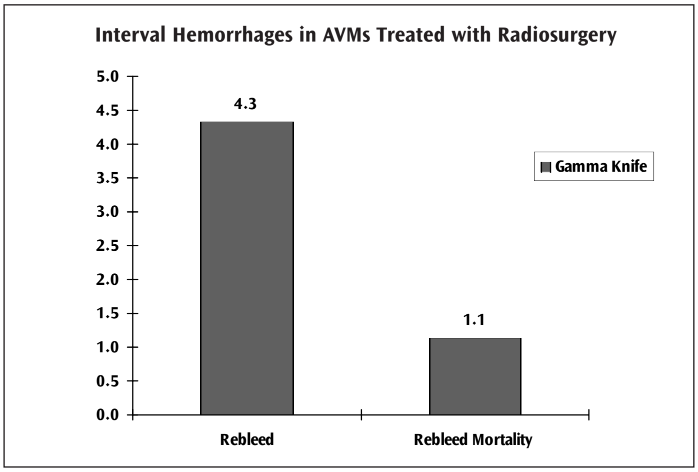

Figure 2. Rebleeding risk and mortality following Gamma Knife® Surgery

At the time of this analysis, results for Gamma Knife® Surgery on a total of 2067 patients with AVMs are reported(Table 1). The obliteration rates vary from 70% to 91% (Mean 78.4%). The corresponding morbidity varies from 0% to 3.8% (Mean 3.6%).[37-40, 41, 42-44] Since the AVM is not removed surgically nor obliterated instantaneously, the risk of delayed complications or hemorrhage - although extremely low - remains until the obliteration process is completed. The risk of rebleeding from an AVM during the latency interval between treatment and obliteration is approximately 4.3% (Figure 2). This level of risk is no greater than if the AVM had been left untreated entirely. Furthermore this risk seems to decrease after the first 6 to 12 months following the radiosurgical treatment. Both radiosurgical and microsurgical series require long-term outcome studies to facilitate comparisons. Some microsurgical series are difficult to interpret since the number of complete excisions performed is not reported and most series tend to exclude those patients who had only subtotal microsurgical removals or required multiple procedures.

There is no consensus in the neurosurgical community regarding the size, location, or type of AVM that may be best managed by microsurgery or radiosurgery. Reported series indicate that between 22-36% of AVMs treated by radiosurgery are greater than 30 mm in average diameter in all dimensions.

Embolization (occlusion of the AVM with materials that directly block the flow of blood through it, or induce thrombus formation and subsequent occlusion) is another alternative to the management of AVM. Despite the fact that this method has been in use for many years its real value in treating AVMs as the single and only modality remains questionable. This is underscored by the fact that a review of available published series [17, 45-71]revealed that primary cure of AVM was achieved only in 3.3% of the cases(Table 2). Complications were seen in 0% to 24% (Mean 8.8%) of the patients, and the average mortality was 1.5%. Embolization may play a role in very selected cases and is more often used in combination with either microsurgery or radiosurgery.

There has been extensive debate in the literature regarding the overutilization of radiosurgery in the treatment of AVMs which are smaller than 3 cm in all

TABLE 2. OUTCOME OF ARTERIOVENOUS MALFORMATIONS FOLLOWING EMBOLIZATION

Treatment modality	*Year*	*No: Cases*	*Agent*	*% Obliterated*	*% Morbidity*
Stein[58]	1977	28	silastic spheres	nr	4
Mullan[63]	1979	28	silastic sponge	nr	4
Wolpert[51]	1979	27	silastic spheres	nr	4
Debrun[68]	1982	37	IBCA	11	19
Vinuela[55]	1983	12	IBCA	0	17
Vinuela[54]	1984	64	IBCA	0	2
van Alphen[50]	1986	17	IBCA	12	24
Merland[49]	1986	67	IBCA	9	10
Andrews[48]	1986	8	IBCA, PVA	0	0
Halbach[47]	1988	31	Balloons	0	3
Pelz[46]	1988	15	IBCA, PVA	0	20
Vinuela[45]	1989	213	IBCA, NBCA, PVA	nr	12
Berthelsen[69]	1990	29	IBCA	10	7
Fox[66]	1990	38	IBCA, PVA, Avitene	0	11
Purdy[60]	1990	51	PVA, Coils	nr	8
Fournier[67]	1991	49	IBCA	14	8
Schumacher[59]	1991	35	PVA, Silk, Gelfoam	0	9
Pasqualin[61]	1991	49	IBCA, threads	0	4
Benati[70]	1992	136	IBCA, threads	0	7
Nakstad[62]	1992	15	PVA, Coils	60	7
Guo[71]	1993	46	IBCA, NBCA, PVA	0	20
Jafar[65]	1993	20	NBCA	0	5
Marks[64]	1993	6		17	0
Wilms[52]	1993	8	NBCA, IBCA	50	13
Grzyska[17]	1993	56	PVA, coils, ethibloc	0	0
Summary Data		**1085**		**3.3**	**8.8**

TABLE 3. OUTCOME OF MANAGEMENT OF SMALL ARTERIOVENOUS MALFORMATIONS

Series	*Year*	*% in Brainstem,Basal Ganglia, Corpus Calossum*	*No:*	*% Obliterated*	*% Morbidity*	*% Surgical Mortality*	*% Latency bleed*	*% Latency bleed Mortality*
Leksell Gamma Knife®								
Coffey[41]	1995	33	90	72	2.5	0	4	2
Pollock[40]	1994	89	65	84	1.5	0	7.7	3.1
Steiner[75]	1992	35	161	83	nr	0	2.3	0.9
Summary Data			**316**	**80**	**2.1**	**0**	**4**	**1.7**
Microsurgery								
Schaller[72]	1997	23	62	98	6.1	0	na	na
Sisti[15]	1993	25	67	94	1.5	0	na	na
Heros[22]	1990	10	47	98	2.1	0	na	na
Spetzler[16]	1986		45	98	2.2	0	na	na
Lussenhop[26]	1984		74	nr	4	0	na	na
Summary Data			**295**	**97**	**3**	**0**	**na**	**na**

diameters or less than 10 cc in volume depending on the classification in use. Unfortunately majority of the literature does not classify results by size of AVM. The papers that do stratify results based on AVM size are summarized in Table 3. [15, 16, 22, 26, 40, 41, 72-75] Whereas size was used to classify these results, location was not. It turns out that the Leksell Gamma Knife® radiosurgical material includes more cases in deep locations. If microsurgical results of an equal number of deep albeit small AVMs were compared the morbidity would undoubtedly be higher. Even if this supposition is not accepted by the reader, it should be remembered that neurosurgeons using radiosurgery treat at least as many and usually more lesions in deep locations such as the brainstem as in the microsurgical series.

Literature is now emerging on the role of GKRS in large AVM's not amenable to surgical excision. Pan *et al* [76] report a 77% obliteration rate at 40 months for AVMs 10-15 cc in volume and 56% obliteration rate at 50 months for AVMs larger than 15 cc. Considering that these patients are excluded from surgical and endovascular options these figures are promising.

Meningiomas

Meningiomas are benign tumors arising from the covering of the brain the '*meninges*', Surgical removal has traditionally been the first line of management for most patients. Meningiomas, however have proved to be difficult to cure, especially in locations at the skull base and when they invade the major dural venous sinuses. The long term outcome of many patients therefore remains morbid especially when the tumor occurs in elderly age groups. Meningiomas present a challenge to the surgeon attempting their total removal, and even when totally removed are notorious for recurrence. The medial sphenoid wing, the petro-clival ligament and the cavernous sinus are anatomical locations presenting special difficulty. In an analysis of 225 meningiomas operated at the Massachusetts General Hospital, it was established that the success of meningioma surgery was directly related to the extent of tumor resection. Whereas the patients undergoing 'total removal' had a 17% recurrence rate at 5 years and 32% at 15 years,

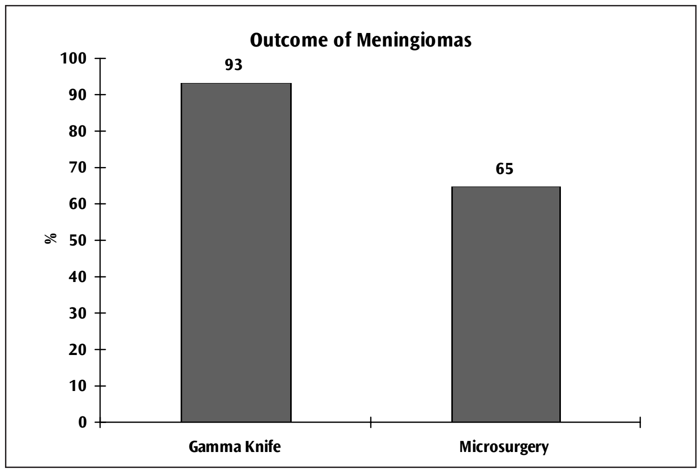

Figure 3. Outcome of meningioma management

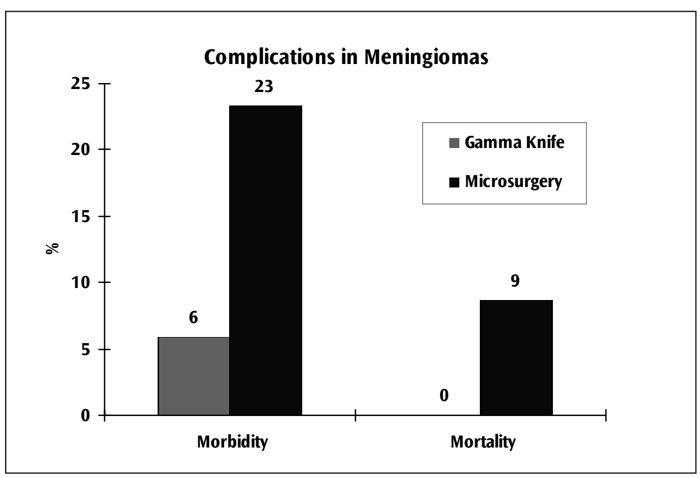

Figure 4. Complications of meningioma management

those with a 'subtotal resection' had a recurrence rate of 37% at 5 years and 91% at 15 years.[77] Fifty-three consecutive cases operated over a 10 year period at the University of Manchester in England with a mean follow up of 5.3 years had a 9.5% recurrence rate if the dural attachment of the tumor was excised with the tumor. The rate of recurrence increased to 18.4% if the attachment was only coagulated.[78] Although every effort should be made to totally extirpate the tumor, the goal of surgery should also be to preserve the quality of life, even if this means leaving residual tumor. Cumulative data from literature[79] revealed that 90% of the convexity meningiomas are completely removed at surgery, by comparison, only 34% of the meningiomas arising from the sphenoid wing were reported as completely removed. Results for 4,082 patients with meningiomas in different locations are included in the present review (Table 4). Complete resection (the accepted criterion for successful

TABLE 4. OUTCOME FOR MENINGIOMAS

Series	*Year*	*# Cases*	*% Shrunk/ Unchanged (Completely Resected)*	*% Recurred (Of total Resections in surgical series)*	*% Morbidity*	*% Mortality*
Leksell Gamma Knife®						
Shin[111]	2001	37	92	8	5	0.0
Stafford[112]	2001	190	91	9	13	0.0
Aicholzer[113]	2000	46	96	4	4	0.0
Roche[114]	2000	80	95	5	4	0.0
Liscak[115]	1999	67	100	0	4	0.0
Kondziolka[116]	1998	66	94	6	13	0.0
Subach[117]	1998	62	90	8	8	0.0
Kurita[123]	1997	25	96	4	4	0.0
Pendl[121]	1997	78	96	4	5	0.0
Hodes[125]	1996	20	100	0	5	0.0
Hudgins[124]	1996	100	90	nr	2	0.0
Nicolato[122]	1996	50	98	2	6	0.0
Tanaka[119]	1996	30	93	2	3	0.0
Steiner[118]	1995	151	89	11	0	0.0
Pendl[120]	1994	37	92	8	7	0.0
Duma[126]	1993	34	100	0	4	0.0
Kondziolka[330]	1991	50	96	4	6	0.0
Summary Data		**1123**	**93**	**6.1**	**5.9**	**0.0**
Microsurgery						
Honeybul[81]	2001	15	47	30	20	0.0
Zevgaridis[82]	2001	62	23	15	6	4.0
Arai[83]	2000	21	nr	5	20	0.0
Ayerbe[84]	1999	286	38	8	nr	nr
O'Sullivan[89]	1997	39	21	5	18	0.0
Samii[87]	1997	21	76	nr	27	0.0
Zentner[88]	1997	19	68	0	11	5.0
De Jesus[90]	1996	119	61	10	27	2.0
Kim[92]	1996	21	48	25	45	9.0
Matheisen[91]	1996	315	17	16	nr	9.7
Samii[86]	1996	180	57	nr	23	3.0
De Monte[93]	1994	41	76	10	27	5.0
Mahmood[94]	1994	276	72	6	nr	nr
Ciric[95]	1993	26	62	13	23	16.0
Marinov[96]	1993	668	63	nr	nr	12.6
Samii[97]	1992	36	75	nr	17	0.0
Al Mefty[98]	1990	24	96	nr	4	8.0
Kleinpeter[100]	1990	44	73	12	34	12.0
Shekhar[99]	1990	45	82	2	0	2.0
Djinjian[80]	1988	30	100	nr	nr	23.0
Hakuba[101]	1988	8	75	10	13	0.0
Jaaskelainen[102]	1986	657	100	19	nr	nr
Jan[103]	1986	161	76	10	30	14.3
Mayberg[107]	1986	35	26	22	31	9.0
Mirimanoff[77]	1985	373	64	32	nr	7.1
Pertuiset[105]	1985	353	nr	4	nr	7.0
Pompili[106]	1981	49	65	10	33	4.0
Yasargil[108]	1980	20	35	25	30	10.0
Konovalov[104]	1979	138	85	nr	nr	11.6
Summary Data		**4082**	**64.5**	**14.8**	**23.4**	**8.6**

surgery) was performed in 17 to 100% (Mean 64.5%) of patients. The worst surgical mortality is reported in a small series of patients all 70 years of age and above [80]and does skew the statistic somewhat in that category. Recurrence rates over a varied period of observation range from 2% (short-term) to 32% (15 years) (Mean 14.8%).[77, 80-108] Surgical morbidity has varied from 0% to 33% (Mean 23.4%) in terms of overall major morbidity. For meningiomas in the petroclival region, the cranial nerve morbidity reported varied 20% to 54%. Surgical mortality averaged 8.6% (Range 0% to 14.3%).

Fractionated radiation has been shown to lower the recurrence rate and relapse of clinical symptoms in several studies. Barbaro *et al* reported a decrease in the rate of recurrence from 40-45% to 25% with the use of fractionated radiation[109]. Taylor reported a decrease in the rate of recurrence from 45% to 18%.[110]

It is logical that if radiation is shown to improve outcome in meningiomas, then focused radiation should combine the benefits afforded by conventional radiation with the advantage of protecting normal structures. This is particularly relevant in the locations where microsurgery is least effective in controlling these tumors. Radiosurgery therefore is recognized today as the optimal treatment modality used in conjunction with microsurgery for meningiomas. Additionally in the subset of cases where for some reason microsurgery is not an option, radiosurgery can be the primary treatment modality.

The endpoint of a successful result in the radiosurgical treatment of meningiomas is either a demonstrable arrest of growth on follow up or a reduction in size. Of the 1,123 patients reported in literature for Gamma Knife® Surgery (Table 4), satisfactory results were obtained in an average of 93% cases.[111-126] (Figure 3). The associated recurrence rates are 0% to 11% (Mean 6.1%). No mortality caused by Gamma Knife® Surgery has been reported and the morbidity figures range from 0% to 13% (Mean 5.9%). Morbidity when reported usually constitutes transient and or reversible deficits.

Radiosurgery is therefore associated with a significant reduction in recurrence rates, and prevents reoperation in up to 90% of patients with relatively low complication rates, even in tumors close to sensitive structures such as the the brainstem or cranial nerves. In economic terms it is clear that a reduction of the population requiring reoperations is a cost containment measure, the true impact of which can be estimated by factoring the costs of repeat surgery, hospital stay, rehabilitation and the loss of work.

Vestibular schwannomas (Acoustic Neuromas)

The microsurgical standards for vestibular schwannomas have been painstakingly established over the years by several surgeons who currently or at the time of retiring from active practice had personal series exceeding 600 patients each, their results clearly set the gold standard to which any others should be compared. Buchmann *et al* [127] and Malis[128] talk of the learning curve for vestibular schwannoma microsurgery and make the point that it takes nearly 200 vestibular schwannoma operations for a surgeon otherwise skilled in microsurgical technique to achieve a high skill level. Based on the current patterns of health care and referral a larger center can take 8 years to accumulate the 200 cases for any given surgeon[127]. In this light blind comparisons of the best microsurgical results to those of Gamma Knife® Surgery are meaningless as they are by no means the expected outcomes in the community. Gamma Knife® Surgery by contrast is less user dependent and the learning process is more collective - sharing of results and dose prescription guidelines on a regular basis levels the playing field for younger centers much more quickly. All of this cannot discount the need to provide surgical relief of impending compression of critical structures in a patient with a large tumor, but the incidentally discovered vestibular schwannoma should not be casually referred to a microsurgeon of limited experience in the expectation of a good outcome. It is fair to say that

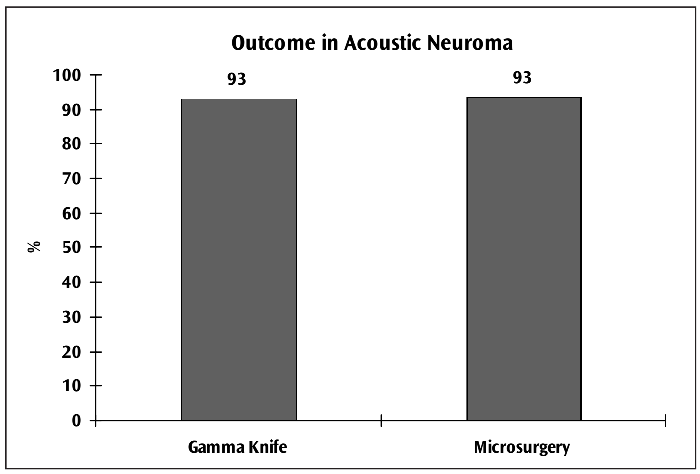

Figure 5. Outcomes of vestibular schwannoma management

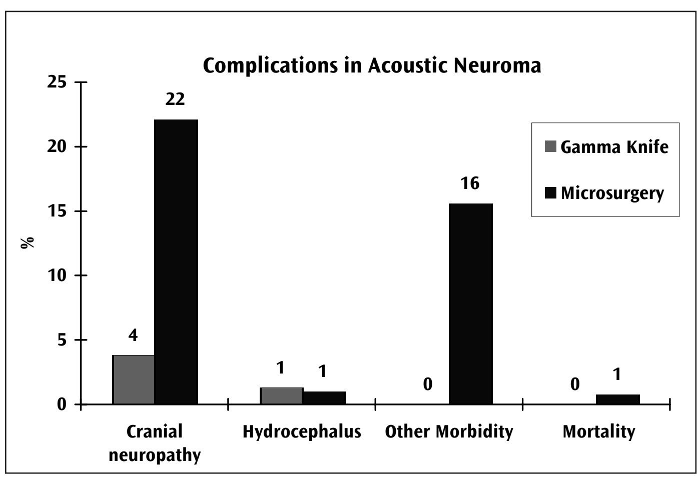

Figure 6. Complications of vestibular schwannoma management

TABLE 5. OUTCOME FOR ACOUSTIC NEUROMAS

Series	*Year*	*No: Cases*	*%Shrunk / Unchanged/ Completely resected*	*%Increased*	*% Morbidity Cranial (except CN VIII)*	*%Morbidity Hearing*	*% Morbidity Hydrocephalus*	*% Morbidity other*	*% Mortality*
Leksell Gamma Knife®									
Bertellanfy[151]	2001	32	91	9	15	21	nr	0	0
Flickinger[152]	2001	190	97	3	4	9	nr	0	0
Petit[153]	2001	45	96	4	0	12	0	0	0
Nakamura[154]	2000	78	81	19	nr	nr	nr	0	0
Prasad[161]	2000	153	92	8	2	35	2	0	0
Roche[155]	2000	37	74	27	9	43	0	0	0
Unger[156]	1999	56	95	5	4	38	0	0	
Flickinger[158]	1996	273	97	1	8	32	3	0	0
Forster[160]	1996	29	83	17	3	nr	0	0	0
Norén[159]	1993	193	94	6	9	77	2	0	0
Summary Data		**1086**	**93.0**	**6.6**	**3.8**	**32.7**	**1.3**	**0.0**	**0.0**
***Microsurgery**									
Sluyter[128]	2001	120	92		21	na	0	47	1.0
Bruzzo[129]	2000	91	nr	nr	4	63	nr	nr	nr
Gjuric[130]	2000	735	92	0.3	17	63			
McElveen[131]	2000	100	81	nr	13	nr	nr	nr	nr
Tonn[132]	2000	508	nr	nr	46	64	nr	19	0.4
Gromley[133]	1997	179	99	1	23	62	3	15	1.0
Nissen[134]	1997	111	91	nr	19	nr	nr	nr	0.0
Sampath[135]	1997	611	95	5	11	nr	nr	27	0.2
Buchman[136]	1996	96	77	6	14	52	0	19	0.0
Gillman[137]	1995	71	79	nr	18	72	0	11	0.0
Glasscock[138]	1993	161	nr	1	1	76	nr	19	0.0
Ojemann[139]	1993	410	89	3	24	85	1	4	0.5
Pellet[140]	1993	178	99	nr	48	63	nr	17	1.8
Ramsay[141]	1993	65	94	nr	15	100	nr	19	0.0
Ebersold[142]	1992	256	97	3	7	81	1	28	0.7
Lownie[143]	1991	12	100	17	18	nr	nr	8	8.3
Hardy[144]	1989	100	97	nr	nr	nr	nr	nr	3.0
Tos[145]	1988	300	nr	nr	34	nr	nr	11	2.0
House[146]	1985	216	100	nr	17	98	nr	12	0.4
Morrison[147]	1984	240	100	nr	42	nr	nr	nr	1.6
Summary Data		**4560**	**93.3**	**2.4**	**22.1**	**71.7**	**1.0**	**15.6**	**0.8**
Patient Review									
Rigby[149]	1997	130	nr	nr	13	93	nr	14	nr
Kane[150]	1995	61	nr	nr	55	86	nr	13	nr
Wiegand[148]	1989	541	nr	nr	60	93	6.5	7	nr
Summary Data		**732**	**nr**	**nr**	**51.2**	**92.4**	**6.5**	**8.7**	**nr**

today it is the microsurgeon that has to make a case to perform an operation on a vestibular schwannoma, failing which all vestibular schwannomas are better managed by Gamma Knife® Surgery.

Patient perspectives on the subject, may be gleaned from the 1989 sentinel study[129] reported by the Acoustic Neuroma Association summarizing the results reported by 541 patients who underwent surgery for acoustic neuromas. 72% underwent translabyrinthine surgery. Complications included meningitis (5.7%), CSF leak (7.2%) and stroke (0.7%). 6.5% of the patients required CSF diversion for hydrocephalus following surgery. Deafness was reported in 93% of the cases. In addition, 80% of the patients had either transient or permanent facial nerve deficits. Recovery of facial function in those that sustained injury to the nerve was seen in only 16%. Postoperative eye problems were seen in 88.5% of cases and 32% of the patients required surgical intervention for the facial palsy. This underscores the fact that although the results from centers of excellence would leave little place for other modalities of management of vestibular schwannomas, the truth is that in the hands of the average microsurgeon there is considerable morbidity with this procedure. Recently other papers[130, 131] have confirmed the findings of Weigand *et al*.

Pooling surgical results from different authors, [127, 132-150], comprising a total experience of 4560 patients a complete resection was achieved in 93.3% of cases (Table 5). The average risk of damage to the facial nerve was 22.1% and other morbidity in the form of CSF leaks, infections, etc. was seen in 15.6% of patients. The mortality associated with current techniques at centers of excellence is low and averages 0.8%. Some of the series reported reflect results of centers with extensive experience and include cases where hearing preservation was attempted. In those centers where hearing preservation was attempted, this goal was achieved in less than 20% of the cases.

The radiosurgical endpoint of treatment is the demonstration of reduced or unchanged tumor size over at least 2 to 5 years. Detailed follow-up studies are now available from Gamma Knife® Surgery centers with experience extending up to 23 years. On average, 93.0% of the patients treated with Gamma Knife® Surgery achieved this result[151-160](Figure 5). Cranial nerve morbidity was seen in an average of 3.8% cases (Figure 6). This could be related to many factors, including tumor volume, dose delivered, dose planning technique, imaging tool selected for tumor visualization, and the length of the cranial nerve irradiated. The specific data elucidating the relative importance of these factors, however, is not available to date. Currently, hearing can be preserved at pre-radiosurgical levels in as many as 51% of patients and the hearing loss where it occurs is gradual so that even patients with compromised hearing in the other ear have the opportunity to learn alternative communication means and adapt to their impending loss. Facial nerve function of up to House-Brackman Grade 1 or 2 is preserved in excess of 90% of patients. There is no risk of other attendant morbidity such as CSF leaks, meningitis or other infections. The need for post-operative CSF diversion is observed in 2% of the patients.

A learning curve exists for the Leksell Gamma Knife® technique as well and improvements in imaging and reduction in prescribed doses have impacted the results (Table 6). The earliest material is reported by Noren and Forster,[159, 160] while later data comes from a number of authors.[151, 152, 154, 156, 161] While the tumor control rate remains constant in the two groups , there is a significant reduction in the cranial nerve neuropathy incidence and one third reduction in loss of auditory function. As the long term follow up of patients treated with lower doses becomes available,[152, 161] the average results of microsurgery for acoustic neuromas are clearly surpassed.

TABLE 6. COMPARISON OF EARLY AND CURRENT RESULTS FOR GAMMA SURGERY OF ACOUSTIC NEUROMAS

Series	*Year*	*No: Cases*	*%Shrunk / Unchanged/ Completely resected*	*%Morbidity Cranial (except CN VIII)*	*%Morbidity Hearing*
Current Gamma Knife series					
Flickinger[152]	2001	190	97	4	9
Prasad[161]	2000	153	92	2	35
Nakamura[154]	2000	78	81	nr	nr
Bertellanfy[151]	2001	32	91	15	21
Unger[156]	1999	56	95	4	38
Summary Data		**509**	**92.4**	**3.9**	**22.9**
Early Gamma Knife series					
Forster[160]	1996	29	83	3	nr
Norén[159]	1993	193	94	9	77
Summary Data		**222**	**92.3**	**8.3**	**66.9**

Pituitary Tumors

The vast majority of surgically treated pituitary adenomas (94%) are now managed by transsphenoidal microsurgical removal , with a minority undergoing craniotomy[162]. Between 1980 and 1997 major series reported a total of 8848 cases.[163-196] This compilation (Table 7) includes data on different types of pituitary adenomas based on their hormonal profile and associated clinical syndromes. There are differences in the way that success in the treatment of these lesions is assessed in the different series. Additionally it must be emphasized that the results for macroadenomas are not reported separately from the microadenomas, thereby

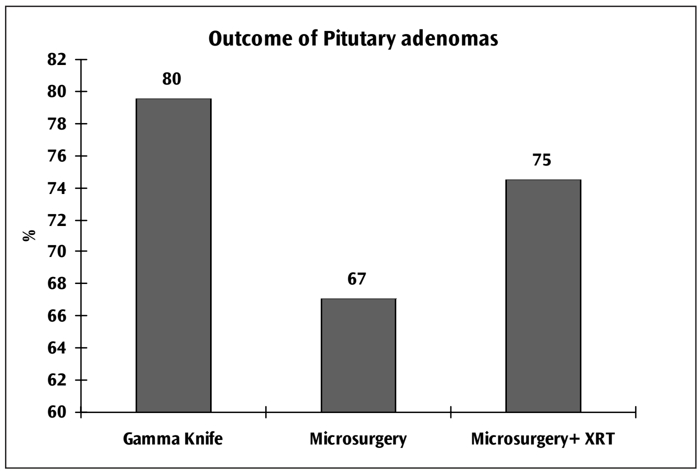

Figure 7. Outcomes of pituitary adenoma management

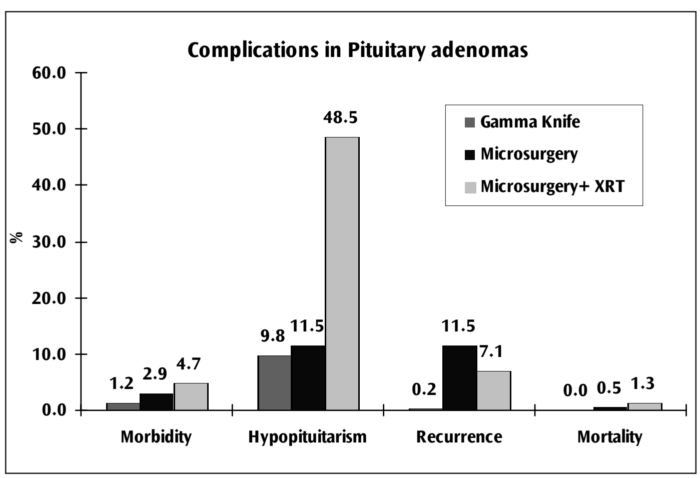

Figure 8. Complications of pituitary adenoma management

TABLE 7. OUTCOME FOR PITUITARY ADENOMAS

Series	*Year*	*No: Cases*	*% Success*					*% Compli-cations*	*% Hypo-pituitarism*	*% Recurrence*	*% Mortality*
			NF	**PRL**	**CUSH**	**NELS**	**GH**				
Leksell Gamma Knife®											
Landolt[219]	2000	20		80				5	0	0	0
Pan[220]	2000	128		80				0	4	0	0
Shin[221]	2000	16	100		50		67	0	6	0	0
Zhang[222]	2000	79					96	1	4	0	0
Ikeda[223]	1998	13	100				90	nr	0	nr	0
Motti[224]	1996	30	50		50		100	0	0	0	0
Park[225]	1996	19	-	71	60	-	71	nr	nr	nr	0
Seo[226]	1995	2	-	-	100	-	-	0	0	0	0
Pollock[230]	1994	35	100		67		72	nr	nr	nr	0
Steiner[37]	1994	46	64	100	66	-	90	nr	0	2	0
Ganz[227]	1993	16	-	66	50	66	75	nr	nr	0	0
Stephanian[228]	1992	16	-	-	50	-	75	11	0	0	0
Rahn[162]	1991	8	-	-	100	-	-	nr	0	0	0
Rahn[162]	1991	51	-	-	82	-	-	nr	55	0	0
Thoren[229]	1991	21	-	-	-	-	48	nr	15	0	0
Summary Data		**500**	**79.6**	**1.2**	**9.8**	**0.2**	**0.0**				
					Range:48-100%						
Microsurgery											
Kreutzer[163]	2001	57					67	3.3	nr	1	0
Abe[164]	1999	78					78	3.8	9	nr	0
Tyrrell[165]	1999	219		85				2.7	0	16	0
Massoud[166]	1997	23	100	100	90	100		17	14	nr	0
Petruson[167]	1997	31			77			0	6	3	0
Yamada[170]	1997	44					87	nr	nr	nr	nr
Bakiri[168]	1996	50			62			nr	10	nr	nr
Giovanelli[171]	1996	932	72	46	87		55	2	nr	nr	1.6
Knappe[169]	1996	55			96			4	45.5	16	0
Massoud[172]	1996	64		90				0.4	nr	43	0.27
Mindermann[175]	1995	136	-	-	-	-	-	nr	nr	10	nr
Petruson[176]	1995	108	92	-	-	-	-	0	12	8	0
Saito[174]	1995	100	89					6	nr	15	3
Wallace[173]	1995	19		42				15	20	nr	nr
Dyer[177]	1994	66	50	86	78	-	0	7	7	nr	1.8
Comtois[178]	1993	126	75	-	-	-	-	nr	nr	21	1.6
Davis[179]	1993	121	-	-	-	-	54	3	18	9	0
Gasser[180]	1993	92	54	60	89	-	57	nr	nr	37	nr
Jaffrain-Rea[181]	1993	33	73	-	-	-	-	nr	nr	27	nr
Laws[182]	1993	2600	-	69	86	43	77	4	nr	15	0.3
Somma[183]	1993	65	-	-	77	-	-	nr	12	10	nr
Tindall[184]	1993	131	-	-	-	-	76	nr	nr	nr	nr
Trainer[185]	1993	48	-	-	67	-	-	15	9	nr	nr
Fahlbusch[186]	1992	222	-	-	-	-	71	nr	nr	7	nr
Scamoni[187]	1991	96	-	49	-	-	-	nr	nr	4	nr
Wilson[188]	1990	1813	-	64	75	21	79	2	nr	6	0.3
Landolt[189]	1988	169	-	-	-	-	70	nr	nr	2	nr
Faria[190]	1982	100	-	61			-	nr	nr	nr	nr
Teasdale[191]	1982	56	-	-	-	-	46	nr	nr	nr	nr
Auoborg[192]	1980	90	-	44	-	-	-	nr	nr	nr	nr
Hardy[200]	1980	912	-	74	-	-	79	2	nr	nr	0.4
Nabarro[195]	1980	162	-	57	25	-	69	6	14	nr	0.6
Post[196]	1979	30	-	70	-	-	-	nr	nr	nr	nr
Summary Data		**8848**	**67.1**	**2.9**	**11.5**	**11.5**	**0.5**				
					Range: 21-92 %						
Microsurgery + Radiotherapy											
Zierhut[202]	1995	138	98	100	100	-	-	1.4	27	5	nr
Clarke[331]	1993	44	-	86	50	-	67	11	23	nr	nr
Fisher[332]	1993	134	55	55	55	55	55	7	nr	9	1.5
Jaffrain-Rea[181]	1993	33	92	-	-	-	-	nr	nr	8	nr
Hughes[333]	1993	160	82	50	75	-	64	4	74	nr	1.2
Summary Data		**509**	**74.5**	**4.7**	**48.5**	**7.1**	**1.3**				
					Range: 50-100 %						

TABLE 8. COMPARISON OF OUTCOMES FOR PITUITARY ADENOMAS MANAGED WITH SURGERY, RADIOTHERAPY OR BOTH

		Microsurgery			Radiotherapy			Microsurgery & Radiotherapy		
Series	*Year*	*# Cases*	*# Recurred*	*% Recurred*	*# Cases*	*# Recurred*	*% Recurred*	*# Cases*	*# Recurred*	*% Recurred*
Zierhut[202]	1995	124	16	13	-	-	-	138	7	5
Comtois[178]	1993	126	27	21	-	-	-	-	-	-
Davis[179]	1993	121	11	9	-	-	-	-	-	-
Fisher[203]	1993	-	-	-	-	-	-	134	12	9
Gasser[180]	1993	92	34	37	-	-	-	-	-	-
Jaffrain-Rea[181]	1993	33	9	27	-	-	-	33	3	9
Laws[182]	1993	2600	395	15	-	-	-	-	-	-
Somma[183]	1993	65	6	9	-	-	-	-	-	-
McCollough[204]	1991	-	-	-	14	0	0	48	1	2
Tran[205]	1991	-	-	-	4	1	25	32	5	16
Grigsby[206]	1989	-	-	-	-	-	-	81	9	11
Rush[207]	1989	-	-	-	28	2	7	-	-	-
Chun[208]	1988	60	9	15	12	6	50	54	7	13
Grigsby[209]	1988	-	-	-	19	4	21	-	-	-
Vlahovitch[210]	1988	89	14	16	-	-	-	46	4	9
Ebersold[142]	1986	42	5	12	-	-	-	50	9	18
Ciric[211]	1983	32	9	28	-	-	-	67	4	6
Erlichmann[212]	1979	-	-	-	23	4	17	111	16	14
Urdaneta[213]	1976	32	12	38	-	-	-	-	-	-
Pistenma[214]	1975	-	-	-	29	12	41	33	6	18
Sheline[215]	1974	29	20	69	23	2	9	80	9	11
Hayes[216]	1971	29	13	45	-	-	-	42	9	21
Kramer[217]	1968	-	-	-	20	9	45	16	5	31
Emmanuel[218]	1966	-	-	-	16	4	25	41	3	7
Summary Data		**3474**	**580**	**16.7**	**188**	**44**	**23.4**	**1006**	**109**	**10.8**

making an important distinction in results based on tumor volume impossible to assess. The range of patients cured varied from 21% to 92%, with the poorest results in Nelson's syndrome (persistent hypersecretion of ACTH after bilateral adrenalectomy). The average figure for successful surgery was calculated at 67.1% associated with a 0.5% mortality and a low morbidity of 2.9%. The average recurrence rate was found to be 11.5%.

The problem of the pituitary adenoma is however rarely solved by surgery alone, residual tumor particularly in the cavernous sinus region requires further management, evidence of dural microinvasion on histology portends high likelihood of recurrence even among patients who have had total resection of tumors[197]. In the specific case of prolactinomas this has been correlated to both the baseline prolactin level and the size of the tumor.[198] The postoperative prolactin levels were found to be normal in 88% of the patients with preoperative levels less than 100 ng/ml. Correlation with preoperative tumor size is demonstrated in the material of Hardy[199] and the reported recurrence rates vary from 17% to 50% for microadenomas and 20% to 80% for macroadenomas.[200, 201] Recurrence is also reported with non-functioning adenomas[202] and the figures varied from 12% in the smaller noninvasive variety to 18% in the more invasive tumors, which also received radiation therapy. The underlying issue is that although surgery, particularly transsphenoidal decompression, provides a rapid and safe method for reduction in tumor bulk and relief of visual and hormonal dysfunction, it has a tendency to fail in the long run.

Conventional fractionated radiotherapy has been used as an adjunct to surgery, resulting in a lower recurrence rate in the combined therapy group (7.1% vs. 11.6%)[145, 178-183, 203-219] Table 8. This improvement is tumor control was at the cost of a high (48.5%) incidence of hypopituitarism (Table 7, 8). Some long term morbidity and mortality related to the adverse effects of radiation notably to the temporal lobes of the brain was reported.

Gamma Knife® Surgery provides a potentially safer and more efficacious means to achieve a precise delivery of radiation to the residual pituitary adenoma or the cavernous sinus and even the empty sella to sterilize the microinvasion of the sellar dura. This technique allows protection of vital brain structures, and from early reports seems to reduce the treatment to response interval. Results for pituitary adenomas using Gamma Knife® Surgery have been reported in multiple series. A total of 500 patients were reported with success rates from 48% to 100% of cases.[37, 162, 220-230] The 100% results are reported in small selective series of patients that have been treated with the current standard of radiosurgery using MRI based localization of tumor 162,[224, 225, 227, 231] whereas the overall figures include some early treatments based on air encephalography to localize the tumor. Thus neither extremes are representative of the true picture. The average figures were found to be 79.6% for successful treatment, measured in terms of reduced tumor size and/or hormonal levels or unchanged tumor size with normalization of the hormone levels. No mortality was reported. The recurrence rates vary from 0 to 2% and although the average value was 0.2%, a longer period of observation and follow up would provide a better estimate.

Once again the choice of treatment depends on the presentation of the patient. Transsphenoidal microsurgery is an effective technique for decompressing optic pathways, obtaining tissue diagnosis, reducing tumor bulk and rapidly ameliorating hormonal abnormalities in a significant number of patients. There are a large number of documented cases where residual tumor exists with or without endocrinopathy, especially in the proximity of the cavernous sinus region. The localized nature of the pathology makes radiosurgery an excellent alternative to fractionated radiation especially for tumors that are 3 to 5 mm from the optic apparatus, as well as tumors that extend laterally into the cavernous sinus. The published results summarized here indicate that radiosurgery is safe and effective and may enhance the overall likelihood of cure for these patients.

Craniopharyngioma

As with other lesions although the Leksell Gamma Knife® was applied fairly early in its history for the treatment of craniopharyngiomas (tumors the arise from embryological remnants within the skull base and region of the pituitary gland) there has been lack of systematic analysis or reporting. The entire literature can be summed up in three published series summarized in Table 9.[231-235] The total number of cases are still very few. A synopsis of the current surgical therapy with and without adjuvant chemotherapy is presented in Table 10.[236-257] The primary reason for seeking alternate therapy is recurrence following surgery, a fact that is only partly brought out in this table. Other issues include the fact complete excision is a difficult surgical goal and the significant impairment of growth potential reported following conventional fractionated radiotherapy. Despite these limitations microsurgery remains the mainstay of therapy for these lesions. When radiation becomes indicated the preferred approach is to use radiosurgery rather than fractionated therapy.

The use of radiosurgery for tumors only a few millimeters from the optic pathways requires a longer evaluation (pituitary and craniopharyngiomas). However, the ability of the Leksell Gamma Knife® to provide steep boundaries to the radiation field and the use of very small beam diameters (e.g. 4 and 8 mm), coupled with specific plugging patterns and shielding

TABLE 9. OUTCOME OF CRANIOPHARYNGIOMAS MANAGED WITH THE LEKSELL GAMMA KNIFE®

Series	*Year*	*# Cases*	*% Shrunk/ Unchanged*	*% Visual Complica-tions*	*% Endocrine Complica-tions*
Chung[231]	2000	31	87	3	0
Mokri[232]	1999	23	74	0	0
Steiner[235]	1995	8	88	0	0
Lunsford[234]	1993	3	67	67	nr
Backlund[233]	1979	9	100	11	n
Summary Data		**74**	**82**	**5.4**	**0**

TABLE 10. OUTCOME OF CRANIOPHARYNGIOMA WITH CONVENTIONAL SURGERY WITHOUT AND WITH FRACTIONATED RADIOTHERAPY

			Complete Resections		**Partial Resection Alone**		**Partial resection plus radiotherapy**	
Series	*Year*	*# Cases*	*% of Total*	*% Recurrance rate*	*% of Total*	*% Recurrance rate*	*% of Total*	*% Recurrance rate*
Rutka & Hoffman[236]	1992	50	100	34	0		0	
Weiss[256]	1989	34	53	33	32	100	15	20
Sweet[246]	1988	28	82	13	18	80	0	
Baskin[249]	1986	67	0	0	0	0	100	9
Stahnke[245]	1984	22	32	29	55	50	14	0
Danoff[251]	1983	14	0	0	0		100	14
Till[255]	1982	49	47	13	n		53	12
Carbezudo[237]	1981	43	30	31	33	86	37	6
Carmel[238]	1981	42	33	50	33	71	33	21
Richmond[243]	1980	8	100	38	0		0	
Thomsett[247]	1980	42	33	29	26	91	40	18
Shapiro[244]	1979	38	58	23	24	78	18	0
Lichter[241]	1977	27	30	38	33	56	37	20
Mc Murry[242]	1977	30	33	20	30	78	37	18
Onoyama[254]	1977	30	0	0	0		100	23
Katz[240]	1975	34	100	26	0		0	
Bloom[250]	1975	33	0	0	0		100	30
Sharma[257]	1974	18	0	0	0		100	0
Hoff and Patterson[239]	1972	41	10	0	44	89	46	63
Bartlett[248]	1971	15	40	50	0		60	33
Kramer[252]	1968	16	0	0	0		100	19
McKissock[253]	1966	45	0	0	0		100	27
Summary Data		**726**	**35**	**28**	**15**	**79**	**50**	**19**

techniques to conform the shape of the dose gradient around vital structures, provides a potentially superior approach to that offered by other modalities.

Metastatic Tumors

Therapeutic endeavors for patients with metastatic disease are aimed at improving the quality of life. These efforts are often thwarted by the progress of the primary disease process and/or the appearance of fresh metastatic deposits. Whatever the modality of treatment for cerebral metastasis, median survivals of more than 12 months are rarely reported. Patchell et. al.[258] demonstrated the superior results of surgical excision followed by radiotherapy in these patients, as opposed to management with radiotherapy alone. Indeed, surgical series usually include post operative fractionated radiotherapy and it is therefore redundant to talk of surgery alone. When reported (Table 11), complete resection and/or improvement in the clinical condition of the patients was seen in 33-97% of the cases (Mean 74.3%).[259-274] The median survival varies greatly due to the preponderance of different tumor types in different series and was 8.9 months on average.[259-263, 265-271, 273-276] The mean 30-day mortality reported by different authors was found to be 8.42%.[259-265, 267, 269-271, 274-276] This is significant in view of the fact that the surgical procedure, even when successful, is essentially palliative. There is also morbidity associated with major neurosurgical procedures in such patients. In the United States, the vast majority of patients diagnosed with a single metastatic tumor to the brain are still treated with external beam fractionated irradiation as the treatment of choice, despite the superior results achieved by craniotomy (for surgically accessible tumors) or radiosurgery (which can be used regardless of tumor location). At present, there are an estimated 170,000 new patients in the United States each year who are diagnosed with a brain metastasis. [277]Some may benefit from a more aggressive management strategy that includes radiosurgery, possibly fractionated radiation therapy and attempts at control of the patient's systemic disease.

Results for management of metastatic brain tumors are reported using the Leksell Gamma Knife® for 2,099 with tumor control rates averaging 91.8 (Range 82 to 100).[37, 118, 278-297] No mortality has been reported in relation to the procedure. The median survivals are comparable to the surgery plus radiotherapy group and the percentage of tumors that are satisfactorily treated seem to be higher. The fact that these results can be obtained with a one stage procedure and that it can also be combined with whole brain radiation therapy if it is suspected that the primary disease is of a nature that will result in further spread make it highly attractive., The morbidity reported in the surgical series is 14.0% against the morbidity of Gamma Knife® Surgery at 4.1%. Coupled with a mortality risk of 8.9% in the surgical group and no reported procedure related mortality with the Gamma Knife® Surgery, radiosurgery seems to provide the same advantage to the patient as surgical removal without the intercurrent risks of a craniotomy.

In a disease where palliation and improvement of the quality of life are the key issues, and where overall

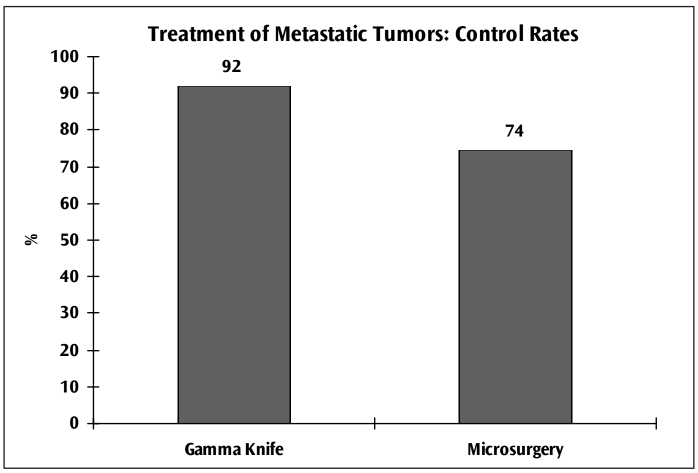

Figure 9. Outcome of metastatic tumor management

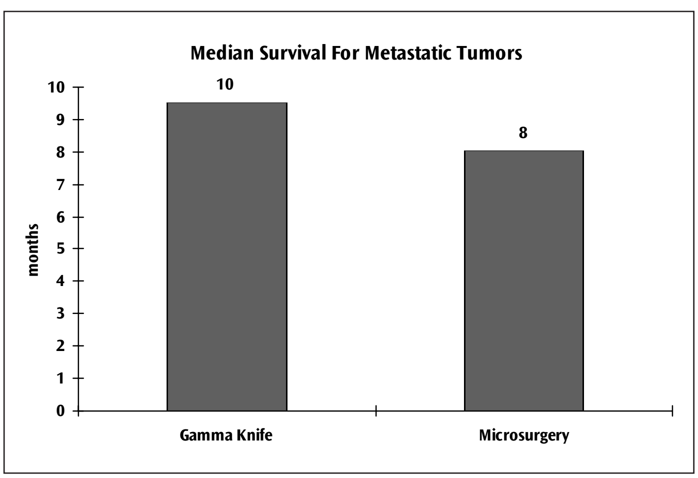

Figure 10. Median survival of brain metastases

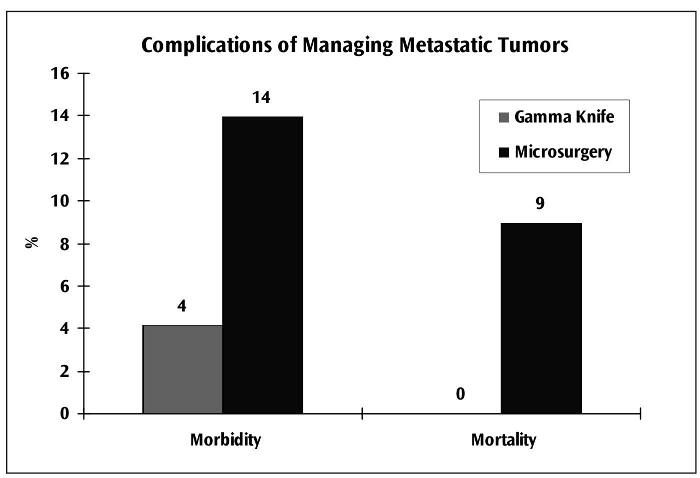

Figure 11. Complications of metastatic tumor management

outcome is dependent on multiple factors and major causes of mortality are usually extra-cranial, radiosurgery emerges as the standard of care for brain metastases, unless acute neurological deficts force the surgeons hand.

Trigeminal Neuralgia

Trigeminal neuralgia is a sharp shooting pain typically involving all or a part of one side of the face, which occurs episodically and lasts any where from a few brief seconds to hours. The genesis of this pain

TABLE 11. OUTCOME OF METASTATIC TUMORS

Series	*Year*	*No: Cases*	*%Disappeared/ Shrunk (Completely Resected)*	*%Increased/ Recurrence*	*%Morbidity*	*%Mortality*	*Median Survival Months*
Leksell Gamma Knife®							
Amendola[278]	2000	22	95	5	5.0	0	8
Amendola[279]	2000	68	94	6	0.0	0	8
Simonova[280]	2000	237	95	5	5.5	0	11
Serizawa[281]	2000	62	95	5	0.0	0	12
Sansur[282]	2000	148	82	18	0.0	0	13
Kim[283]	2000	53	83	17	0.0	0	9
Payne[284]	2000	21	100	0	0.0	0	8
Nakagawa[285]	2000	51	94	6	4.0	0	8
Firlik[286]	2000	30	93	7	0.0	0	9
Chen[287]	2000	190	92	8	5.0	0	9
Peterson[288]	1999	73	90	8	nr	0	12
Muacevic[289]	1999	56	96	4	8.9	0	8
Lavine[290]	1999	45	96	4	7.0	0	8
Schoeggl[291]	1999	97	94	6	2.0	0	nr
Seung[292]	1998	55	89	0	7.0	0	8
Shiau[293]	1997	100	93	7	4.0	0	11
Kim[294]	1997	77	86	13	4.4	0	10
Steiner[118]	1996	100	90	3	nr	0	10
Flickinger[295]	1994	116	85	15	1	0	9
Fukuoka[37]	1993	160	95	3	nr	0	6
Kihlstrom[296]	1993	235	94	6	nr	0	9
Rand[37]	1993	56	100	0	nr	0	nr
Somaza[296]	1993	23	91	9	nr	0	9
Coffey[297]	1991	24	83	0	nr	0	10
Summary Data		**2099**	**91.8**	**7.1**	**4.1**	**0.0**	**9.5**
			Range: 82-100%				
Microsurgery							
Wronski[275]	2000	91	nr	49	27	6	7
Saitoh[259]	1999	24	83	17	nr	8	7
Wronski[260]	1999	73	55	49	nr	3	8
Andrews[276]	1996	25	nr	nr	nr	nr	13
Nakagawa[262]	1994	89	89	11	nr	4	12
Noordjik[263]	1994	32	nr	nr	40	9	10
Penar[264]	1994	32	97	3	6	3	nr
Bindal[261]	1993	26	88	12	8	0	8
Drapkin[265]	1993	52	69	31	nr	2	6
Burt[334]	1992	185	62	24	nr	nr	nr
Chee[273]	1990	19	63	nr	nr	nr	3
Ferrara[274]	1990	100	88	12	nr	6	13
Kitaoka[272]	1990	12	33	67	nr	nr	nr
Patchell[258]	1990	48	75	17	nr	2	19
Salcman[266]	1990	208	nr	nr	nr	nr	4
Sause[335]	1990	77	nr	nr	4	nr	10
Sundaresan[267]	1990	125	87	13	nr	6	9
Kelly[336]	1988	44	nr	nr	11	0	nr
Mandell[337]	1986	35	86	14	nr	9	16
Yardenei[338]	1984	74	nr	nr	nr	15	8
Chan[268]	1982	57	89	nr	nr	nr	6
White[269]	1981	122	nr	nr	nr	6	7
Dosoretz[339]	1980	43	nr	nr	nr	nr	9
Winston[340]	1980	79	nr	nr	5	10	6
MacGee[270]	1971	27	56	nr	nr	26	6
Lang[271]	1964	208	67	nr	nr	22	6
Summary Data		**1907**	**74.3**	**23.3**	**14.0**	**8.9**	**8.0**
			Range: 33-97 %				

syndrome is irritability of the 5th cranial nerve or the trigeminal nerve. Classical trigeminal neuralgia occurs without any physical cause for this irritation of the nerve such as tumor or AVM. Several modalities exist for providing relief to patients suffering from this excruciatingly painful condition, which in its severe form can be totally disabling. Medical therapy is usually the first line of attack. Medications such as Dilantin (Phenylhydantoin), Tegretol (Carbamazepine) or Lioresal (Baclofen) can provide relief in most patients. The dosage of these medications need to be titrated to the response of the patient. Besides the pharmacological side-effects of these agents, there remains the problem of failure and tolerance, that then requires other modalities of treatment.

The other classical approaches are surgical and can be divided into the anterior percutaneous approach to the trigeminal ganglion which can be treated with anhydrous glycerol, compressed with a balloon, or its rootlets can be thermocoagulated with radiofrequency current, and the posterior microvascular decompression and rhizotomy approaches. For the purpose of this review we focus on microvascular decompression and pitch the results of radiosurgery against it as both procedures are essentially aimed at the same anatomical region of the trigeminal complex and may perhaps share mechanisms of effect as well. Microvascular decompression was started by Gardner[298] based on a hypothesis first proposed by Walter Dandy.[299] The real popularity of the procedure is attributable to Janetta[300], who has the largest single series of cases. It is in his hands and those of many others a very effective and safe procedure that provides lasting relief. Several microsurgical series are reported over the years with observation periods of up to 10 years, showing that the procedure is successful in 77 percent (range 62 - 92%) of the patients.[300-317] There is very low mortality (0.5%), but definite morbidity associated with the procedure. Primarily the morbidity pertains to the sensory function of the trigeminal nerve itself (range 3-29%), the other nerve at risk is the 8th (hearing) (range 4-34%). Other complications (range 0-19%) include infections, hemorrhage, CSF leak, thrombosis of dural sinuses, respiratory and cardiac peri-operative complications, to name a few. The details of these aspects are provided in Table 12.

Leksell's motivation for developing the Leksell Gamma Knife® was the treatment of pain. The first patient treated with radiosurgery in 1951 was one with

TABLE 12. OUTCOME OF TRIGEMINAL NEURALGIA

Series	*Year*	*# of cases*	*% Success*	*% Mobidity trigeminal*	*% Mobidity hearing*	*% Mobidity Other*	*% Mortality*
Leksell Gamma Knife®							
Maesawa[318]	2001	220	75	10	0	0	0.0
Brisman[319]	2000	174	81	3	0	0	0.0
Chang[320]	2000	15	87	12	0	0	0.0
Nicol[321]	2000	42	95	17	0	0	0.0
Pollock[322]	2000	100	74	8	0	0	0.0
Rogers[323]	2000	54	93	10	0	0	0.0
Kondziolka[341]	1998	106	94	10	0	0	0.0
Young[342]	1998	110	97	3	0	0	0.0
Regis[324]	1995	20	85	5	0	0	0.0
Summary Data		**841**	**84**	**8**	**0**	**0**	**0**
Microsurgery							
Barker[300]	1996	1204	74	2	1	4	0.2
Cutbush[317]	1994	109	82	11	6	7	0.9
Sun[316]	1994	61	77	7	2	nr	0.0
Aksik[315]	1993	92	92	nr	2	4	2.2
Zakrewska[314]	1993	65	62	22	6	nr	0.0
Klun[313]	1992	178	88	nr	0	2	1.7
Sindou[312]	1990	120	79	nr	nr	nr	nr
Bederson[310]	1989	166	82	3	3	27	0.0
Dahle[311]	1989	57	75	12	2	4	1.8
Burchiel[309]	1988	36	70	25	nr	nr	0.0
Szapiro[308]	1985	68	88	7	4	12	1.5
Apfelbaum[343]	1984	289	70	30	2	7	1.0
Barba[305]	1984	37	73	5	0	14	0.0
Kolluri[306]	1984	72	78	7	19	35	0.0
Zorman[307]	1984	78	91	nr	3	14	
Breeze[303]	1982	52	71	12	8	23	0.0
Rushworth[304]	1982	17	94	18	6	nr	0.0
van Loveren[302]	1982	50	66	16	12	4	0.0
Ferguson[301]	1981	24	71	4	0	21	0.0
Summary Data		**2775**	**77**	**8**	**3**	**8**	**0.5**

trigeminal neuralgia, at that time the source of the radiation was an ortho-voltage X ray machine. Since then there have been significant advances in delivery of radiation (Leksell Gamma Knife®) and localization of the nerve (MRI). The target for radiosurgery is the cisternal portion of the trigeminal nerve and its root entry zone in the brainstem. Data is reported on 841 cases treated for trigeminal neuralgia with the Leksell Gamma Knife® in literature. With one treatment pain relief for more than two years without recurrence is now reported in 84 percent of cases. Morbidity pertaining to the trigeminal nerve remains low (average 8%), and no other morbidity or mortality is reported.[318-326] There have been cases that have been treated a second time for recurrent pain as well. The possibility to treat this disorder without a craniotomy is appealing since there are recurrences and primary failures with microvascular decompression in a significant number of cases. The choice of method remains a multi-factorial decision but patients suffering from trigeminal neuralgia today should be offered the option of radiosurgery along with microsurgery.

CONCLUSION

Neurological surgeons and their colleagues are continuing to look for new, safer, cost effective, and less invasive treatments to enhance patient survival, improve patient outcomes, reduce hospital stays, lessen hospital and physician based costs, eliminate perioperative mortality, contain morbidity and allow patients to resume their normal lifestyle quickly. Although surgery offers immediate relief for many space occupying lesions in the brain, it carries definite risks including those to the life of the patient, as well as the likelihood of recurrence and failure to cure in the long term. Often surgery in itself aims to palliate and not cure a patient's condition. Radiosurgery is rapidly being established as a safe and effective adjunct and in selected cases a fair alternative to microsurgery. Recent articles have addressed the economic aspects of the various modalitites of treatment making a strong case for the economic viability,[327, 328] especially of the Leksell Gamma Knife® where it has been applied.[327]

Recognized as an important neurosurgical tool, the specific role of Gamma Knife® Surgery as an adjunct or alternative to microsurgery has become better defined each year. Both large personal series of individual authors and clinical trials for some of the indications are now available to help in this regard. The arrival of the Leksell Gamma Knife® C with its automated positioning system represents the next logical refinement in the tool itself. This allows the treating team to deliver dose to the target in a more homogenous manner using multiple small size collimators. The end result is an intensity modulation of the beam which could open up new clinical frontiers.

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