

Health Economic Aspects of Gamma Knife Radiosurgery



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Introduction

Cost containment is an essential issue in health care, and treatment methods that are based on outpatient procedures or short-term hospitalization are gaining momentum in the current environment of decreasing ward capacity. Neurosurgery is a good example of this development, with a striking trend towards minimally invasive methods. Neuronavigation allows highly targeted microsurgical interventions, endoscopic surgery has become an essential tool to reduce the operative trauma, and embolization and coiling have replaced many surgical indications for cerebral AVM and aneurysms.

Similarly, the widespread implementation of Gamma Knife radiosurgery has started to replace previously invasive resections of AVM, skull base tumors, acoustic neuromas, and brain metastases. While cost considerations may not directly influence individual treatment decisions, economic comparisons can be highly relevant in the regional determination of ward capacity.

The current review focuses on Gamma Knife radiosurgery and summarizes various economic estimations in the context of current medico-economic trends. The economic impact of radiosurgery in public health systems within the now adjacent fields of neurosurgery, radiotherapy, and oncology is discussed.

Macro environment

In general, Europe has a publicly regulated universal health-care system, with only a small proportion of patients being privately treated. In 2008, EU member states used 8.3% of their GDP on average on health-care expenditure, ranging from around 6% in Cyprus and Romania to more than 11% of GDP in France. This compares with 16% in the United States. Across the EU, per capita health spending between 1998 and 2008 is estimated to have increased in real terms by an average of 4.6% a year, thereby growing more quickly than GDP per capita in most European countries.¹ European countries increased their total annual expenditure on health per capita to an average of € PPP 2,192 (€ PPP 671–4,294) in 2008.¹ As a result of the recent recession in many European countries, the ratio of health expenditure to GDP has increased sharply. In Ireland and the UK, increases in overall health spending have even outpaced economic growth.

As one of few countries that successfully controls its health-care expenditure, Germany has effectively limited costs through spending caps for sectors and individual providers, through reference prices for pharmaceuticals, and through reductions in ward capacity.² This reflects a general tendency in all European countries to reduce the number of hospital beds and to shorten the hospital stay in order to compensate for increasing costs. In Europe, the number of hospital beds decreased from an average of 7.3 per 1,000 population in 1995 to 5.7 in 2008, while the average length of stay in European hospitals fell from 8.3 days in 2000 to 7.2 days in 2008.¹ In Sweden in 2006, there were 2.2 hospital beds per 1,000 population, reflecting a 45% reduction since 1993. The number of hospital beds in Germany fell by 24% between 1992 and 2009 (2009: 6.1 beds/1,000 population), while the number of patients increased by 17% (2009: 217 cases/1,000) (Source: Statistisches Bundesamt Deutschland). The trend was even more drastic in the UK, where between 1984 and 2004 ward capacity was reduced by 31%, accompanied by a 57% increase in inpatients. Between 2006 and 2009 the number of NHS beds fell further.

A reduction in hospital resources results in higher saturation of the existing system, greater bed occupancy, and a reduced length of stay on the ward. Many public systems work at maximum capacity and

a further shortening of hospitalization will rather increase the total costs due to higher patient turnover with an increasing relative proportion of high-cost components, such as diagnostic services and immediate postoperative care. Diagnosis-related remuneration has contributed to a greater reluctance to engage in maximally invasive interventions, which would involve higher risks for intensive care treatments and potentially costly therapy-related complications.

In summary, health expenditure is rising, causing both political concern and public outrage when necessary restrictions are implemented. There has been a general trend towards reducing the number of hospital beds and shortening the length of stay in hospitals. Although these developments concern very large systems, they also concern the other end of the spectrum, the actual treatment unit, since one of many consequences is an increasing trend towards minimally invasive interventions to allow shorter hospitalization. In general, these new types of interventions require new investments in specific technology as well as specialized training.

Cost calculation and capacity

It is important to bear in mind that costs in health care generally cover the entire sequential chain of diagnostic and therapeutic components, which involve a large group of coordinated staff. This staff unit has a quantitatively defined capacity for the medical services it provides. The individual costs fall when the medical unit operates close to its maximum capacity. Hence costs for medical treatments vary with the number of annually treated patients per unit. In general, public health-care systems function close to their maximum capacity and therefore costs are generally considered to be constant. This is not the case for treatment units operating below or above their maximum capacity.

Surgery has to be regarded as a sequential process that comprises a chain of events consisting of preoperative imaging, anesthesia, the operation, postoperative intensive care, ward care, etc. The essential characteristic of these activities is their inherent sequence. The overall capacity of this sequential treatment unit is determined by the weakest link in this series of processes, which typically determines the output of the entire unit. Hence the relationship between staff and output is not necessarily linear, something which is rarely considered.

A neurosurgical team of approximately 24 members with nurses and surgeons in the operating room and on the wards can be regarded as the minimum staff size allowing the full sequence of surgical therapy, with an approximate maximum treatment capacity of 40 patients per month. Staff reductions below this "minimum production unit" of 24 members create operational disruptions that jeopardize the entire necessary sequence for surgery. Potential increments in activity above the maximum capacity will require new investments in an entire new sequential staff team and equipment. This second team will function at a lower cost/benefit ratio until maximum capacity is reached again.

Accordingly, the medical unit will operate with ideal cost effectiveness only close to its maximum output. On the other hand, fluctuations in occupancy will cause unpredictable situations and considerable nonlinear variations in cost effectiveness particularly when activity above the defined maximum output capacity is required. The results are oscillations between high costs and low efficiency. This is the typical complaint against public health systems that are dimensioned to function close to their maximum capacity.

In a neurosurgical unit with high output close to maximum capacity, the implementation of radiosurgery "absorbs" some fluctuations in workload. The surgical unit is enabled to function closer to maxi-

mum capacity with improved cost efficiency through a proportional shift to minimally invasive Gamma Knife treatments and also through a reduction in perioperative morbidity, which will be outlined in detail. Apart from the occupancy rate mentioned above, the combined costs for a surgical/radiosurgical unit are related to the proportion of highly invasive interventions due to the resulting costs for morbidity, intensive care, and secondary treatments. Savings for the operative unit are achieved through a focused avoidance of some highly invasive interventions, which can be carried out using radiosurgery with no loss of medical efficacy. Hence radiosurgery can be expected to have a positive impact on relative costs for the entire surgical unit, provided the treatment volume is sufficiently high.

The consequence is that, independently of the direct costs for Gamma Knife treatments, the implementation of radiosurgery has a significant impact on the overall costs of the entire treatment system. These contributing systemic factors have so far not been considered in economic evaluations of surgical and radiosurgical systems. The nonscientific comparison of the costs of neurosurgical units in Sweden between 2004 and 2006 indicates a trend towards 12–25% lower costs for the only neurosurgical unit with an integrated Gamma Knife, although a multifactorial analysis has not been carried out and a more analytical approach would certainly be required to confirm these data.

Various perspectives on costs

The estimation of medical treatment costs is complex since they vary substantially, depending on the hospital's or the insurer's or the socioeconomic perspective. It is obvious that there is major variability in treatment costs for a defined medical condition, depending on the treatment option chosen, the geographical location, and time.

The direct hospital-related costs for therapeutic interventions comprise investment and capital costs, staff and imaging, diagnostic services, and ward care. The costs that are relevant for the insurer are pertinent to the associated risk of secondary morbidity, the need for ancillary treatments, and unpredicted readmissions. The socioeconomic perspective focuses on lost workdays, which are generally of lesser concern for the hospital or the health insurer. These different economic aspects are rarely considered separately, but should ideally be calculated in all comparative cost/benefit analyses.

Cost calculations in neurosurgery

Cost estimations for neurosurgical tumor resections show a considerable range, depending on time and region: The average hospital charges for an open neurosurgical tumor resection in the US were calculated at \$27,523 (1997 including WBRT),³ \$28,438 (1996),⁴ and \$30,461 (1995).⁵ In 2008, the mean cost of microsurgery for acoustic neuroma at the Mayo Clinic was \$23,7886 and in Canada in 2009 €14,561.⁷ In the Netherlands in 1997, the direct costs of microsurgery for acoustic neuroma amounted to DFL 20,072, equivalent to \$9,634.⁸

In Germany in 2003, the average overall costs for microsurgery of meningiomas, acoustic neuromas, metastases, and AVMs were calculated at €10,814,⁹ but 70% of surgical patients needed ancillary inpatient therapy, i.e., rehabilitation or radiotherapy, and 20% of the microsurgically treated patients required an unplanned readmission after discharge.⁹ The resulting total costs for microsurgery including these additional expenditures were €15,242.⁹ This valuable analysis demonstrates the quantitative impact of secondary costs due to unpredicted readmissions and ancillary treatments, which typically remain unconsidered when only direct treatment costs are compared.

Cost calculation for Gamma Knife radiosurgery

Gamma Knife has provided a minimally invasive treatment alternative for many conditions that previously required open surgery or fractionated whole brain radiation. The Gamma Knife treatment allows a reduction in ward capacity, in particularly in high- cost areas such as postoperative and intensive care, but the implementation of radiosurgery requires investments in training and equipment.

The costs for a Gamma Knife service comprise the initial investment and service, the treatment including costs for staff, imaging, and a very small ward with limited facilities. As previously outlined, the overall staff size needed for a neurosurgical unit operating on about 40 patients per month is 24. The comparable minimum staff size of a Gamma Knife unit for the same number of 40 treated patients per month is 6, comprising two physicians (a neurosurgeon and/or radiation oncologists), one physicist, two nurses, and one secretary.

The operating costs of a Gamma Knife unit in Europe are currently approximately €2.25 m per year.⁹ A considerable part of the total costs are fixed and independent of the number of treated patients. As outlined above, the relative costs for a radiosurgical treatment will decrease up to the maximum number of patients that can be handled by the staff involved. Hence the resulting individual treatment costs per patient are dependent on the occupancy of the radiosurgical unit, ranging from approximately €15,000 when 150 patients are treated annually to €4,500 when 500 patients are treated, which has to be considered to be close to the maximum output for one radiosurgical staff unit. With the same Gamma Knife it is technically possible to treat a higher number of patients, although the necessary time will require a second staff unit.

Based on a total of 284 annually treated patients and estimated annual Gamma Knife operating costs of €2,249,223, Wellis and colleagues calculated the costs for an individual radiosurgical treatment at €7,920. In direct comparison, these resulting Gamma Knife treatment costs were significantly lower than the expenses for a corresponding surgical treatment.⁹ The direct costs for radiosurgery range (depending on the time period and the regional environment) from \$20,209 (US 1995) to ca €4,400 (Netherlands 2011:personal communications). Extremely low costs are only possible when high

numbers of patients are treated or in the rare circumstances of public cost calculations, which are not based on a return on investment.

A recent economic analysis comparing Gamma Knife and Linac radiosurgery demonstrated an exponential decrease in cost per patient, depending on the number of patients treated.¹⁰ It was assumed that the Linac treatment could be employed for other radiotherapy needs when it was not used to treat neurosurgical patients. This variable use allowed a function closer to the modified Linac's "maximum output" and lowered the costs. This was an advantage when only a small number of patients with radiosurgical indications were treated.

However, it was calculated that the Gamma Knife became more cost-effective than the Linac when more than 150 patients annually were treated, since Gamma Knife radiosurgery requires less time and staff resources than a stereotactic Linac. The resulting savings were estimated to be 359 Australian dollars (about €295) per Gamma Knife-treated patient.¹⁰

Treatment of AVM

Cerebral AVM can cause potentially devastating bleeding in the brain. In order to prevent hemorrhages, an AVM can be treated by endovascular embolization, open neurosurgical resection, or Gamma Knife radiosurgery. Embolization is rarely complete and therefore generally not sufficient; it is mostly used to reduce the size of the AVM. While the surgical treatment is considered to be immediately curative, it may be associated with more serious side effects and morbidity. Gamma Knife radiosurgery is less invasive, but has a slightly lower success rate. It is associated with a latency period of 2–3 years until the final obliteration of the AVM is achieved. A cerebral bleed can theoretically occur during this latency period, with a risk of 2–3% per year.

The resulting comprehensive costs for treatment and potential side effects after surgery or radiosurgery of AVM have been translated into economical terms using the quality-adjusted life-year assessment (QALY) in a Canadian study by Porter and colleagues (1997).¹¹ The term QALY has been created to measure a treatment outcome by quantification of the combined quantity and quality of life, a year in perfect health being defined as QALY 1. Porter and colleagues estimated the total acute care cost (procedure plus hospital stay) to be \$15,723 for surgery and \$4,185 for radiosurgery.¹¹ Despite the lower immediate treatment-related costs for radiosurgery, surgery confers a long-term clinical benefit of 0.98 QALYs for the treatment of small, operable brain AVMs due to the different cure rates and the inherent latency of the radiosurgical effect.¹¹

However, since the costs in this study were closely related to the treatment outcome, the cost/benefit ratio changes in favor of radiosurgery when the rate of permanent neurological morbidity resulting from surgery exceeds 12% or when the surgical mortality rate exceeds 4%.¹¹ This calculation actually reflects daily clinical practice, where radiosurgery is generally preferred for deep-seated or complicated AVMs for which the risk level for surgery is considered to be high. The surgical morbidity rate can vary considerably and is related to the anatomical location of the AVM, its size, and form of venous drainage. A recent literature review of 25 published surgical series after resection of cerebral AVM provides an estimation of the current operative risks: the data comprising 2,452 patients with AVM showed an average postoperative mortality of 3.3% and a permanent postoperative morbidity of 8.6%, which is very close to the general socioeconomic cost-effectiveness of radiosurgery.¹²

Acoustic neuroma

Acoustic neuromas are benign tumors located in the cerebello-pontine angle close to cranial nerves and the brain stem. Growth of these tumors can cause neurological symptoms and treatment is generally necessary. The removal of acoustic neuromas is surgically highly challenging and the operative resection is still associated with significant perioperative morbidity. As a treatment alternative, Gamma Knife radiosurgery is increasingly used in the treatment of acoustic neuroma, allowing long-term tumor growth control. The outcome with respect to local tumor control of small acoustic neuromas is generally considered to be comparable after surgery and Gamma Knife radiosurgery. Several prospective and retrospective studies, however, demonstrate a significantly superior functional outcome after Gamma Knife treatment compared to surgical resection with regard to facial movement, hearing preservation, and quality of life.¹³

The Mayo Clinic analyzed the initial and follow-up costs in patients with unilateral, previously unoperated vestibular schwannoma who underwent resection or radiosurgery between 2000 and 2002, showing a cost benefit of about 32% in favor of radiosurgery. The mean cost of microsurgery was \$23,788 compared with \$16,143 for the radiosurgical group.⁶

Five years earlier a comparable European study had shown a similar significant cost benefit of 28.9% in favor of Gamma Knife after comparing the treatment costs of microsurgery vs. radiosurgery for acoustic neuroma patients.⁸ Direct costs for microsurgery amounted to DFL 20,072 and for Gamma Knife to DFL 14,272.⁸ The average total hospital stay from the day of surgery of patients treated by microsurgery is 13 days, nearly 11 days of normal care and over 2 days of intensive care, while Gamma Knife requires an average stay of 1.6 days. The mean costs of hospitalization from the day of the treatment were almost DFL 9,000 per patient treated by microsurgery, compared to only DFL 265 for Gamma Knife radiosurgery.⁸

Indirect costs were determined as the value of lost production due to patients being unable to work. Patients in paid employment were absent from work for 3 months after surgery and one working week after radiosurgery.⁸ The resulting indirect costs were DFL 16,400 for surgery and DFL 1,020 for Gamma Knife. Given a similar clinical long-term outcome, which can be assumed from numerous other publications but was not analyzed in this study, it was demonstrated that radiosurgery was significantly more cost-effective than microsurgery for a small acoustic neuroma.⁸ Another recent study calculated an average of 160 (± 158) lost workdays after open surgery for benign skull base tumors vs. 8.0 (± 9) days for Gamma Knife, which contributes considerably to the beneficial effect of Gamma Knife radiosurgery in the socioeconomic cost calculation.¹⁴

A cost analysis within the Canadian health-care system put the mean cost for microsurgical removal of a unilateral acoustic neuroma at €14,561, compared to Gamma Knife radiosurgery at €17,978.⁷ Although the surgical costs in this series appear comparable to the other series mentioned, the Gamma Knife costs in this Canadian study must be considered to be relatively high since patients were sent abroad to the New England or the University of Pittsburgh Gamma Knife Centers in the US. In addition, indirect costs for ancillary treatments and side effects were not taken into consideration, making a direct comparison with other studies impossible.⁷

The considerable regional variation in costs complicates matters further. For example, in Taichung, Taiwan, the direct costs for open surgery of benign cranial base tumors were calculated to be only USD 5,837 and thus lower than the costs for Gamma Knife.¹⁴ These low immediate surgical costs appear to be currently irreproducible in Europe or the US.

The economic aspects of mortality and long-term morbidity after surgical resection of an acoustic neuroma are not included in the surgical cost calculations referred to; however, analysis of 2,643 surgical excisions of acoustic neuromas performed by 352 surgeons in 265 American hospitals showed a mortality of 0.5% and discharge to long-term care in 1.2% of cases. Of patients who had surgery at the lowest-volume-quartile hospitals, as many as 1.1% died and 12.3% were not discharged directly home.¹⁵

Brain metastases

A recent European prospective series (2010) attempted to estimate the cost per life year of patients with brain metastases who were treated with either best supportive care (BSC) or primary radiotherapy (RT) and/or surgical resection. The estimated cost per life year for the combined treatment groups was €43,955.¹⁶ In the Netherlands, the average annual treatment cost per patient with unresectable advanced non-small-cell lung cancer (without brain metastases) was approximately €32,000.¹⁷

The majority of European patients with brain metastases are still treated with conventional fractionated radiotherapy (WBRT); however, immediate side effects, limited prognosis, and lack of local efficacy have recently been the subject of intense discussion. Although conventional fractionated radiotherapy of brain metastases is a relatively inexpensive treatment, its limited efficacy has to be taken into account in the cost/benefit analysis: the local tumor control after fractionated WBRT of brain metastases has been reported to be between 24 and 38%,^{18,19} with a resulting median survival of between 84 days and 4.1 months.²⁰⁻²⁴

In 1997, Mehta et al. made a cost/benefit estimation of conventional fractionated radiotherapy (RT), surgery, and radiosurgery (RS) for patients with single brain metastases, based on a review of the medical literature for clinical data and computerized billing records of all patients for the estimation of costs.³ The median actual costs for these three procedures were \$6,500 for RT, \$15,102 for RT plus RS, and \$22,018 for resection plus RT. Based on a median survival of 21 weeks for whole-brain external beam radiotherapy, 42 weeks for surgery plus whole-brain external beam radiotherapy, and 56 weeks for radiosurgery plus fractionated radiotherapy, the costs in dollars per life year of median survivorship were \$16,250 for RT alone, \$13,729 for RS plus RT, and \$27,523 for resection plus RT.³ Hence, according to this study, a surgical resection required a 1.8-fold increase in cost, compared to radiosurgery.³

A similar American comparative cost analysis was based on data from the 1992 'Medicare Provider Analysis and Review' file for hospital costs for microsurgery and Gamma Knife radiosurgery comprising a detailed financial survey, including capital costs, labor expenses, and operating costs for Gamma Knife,⁵ which also considered costs derived from specific complications reported in the literature.²⁵⁻²⁷ Gamma Knife involved lower uncomplicated costs per procedure and resulted in lower treatment morbidity. Hence the costs per life year were 30% lower for radiosurgery than for the comparable surgical resection.⁵ While the average cost for Gamma Knife treatment in this early study from 1995 has to be regarded as relatively high by current standards, the costs for the surgical tumor resection were \$30,461 and comparable to the previously cited study by Mehta. Similar cost effectiveness with a 30% cost advantage for radiosurgery over surgical resection had also been demonstrated by others.⁴

A very recent study (2012) analyzed clinical trial data, including detailed costs, to compare the cost-effectiveness of Gamma Knife radiosurgery with surgical resection in the treatment of brain metastases from the perspective of Germany's public health system.²⁸ 196 patients with balanced prognostic factors were treated either with Gamma Knife radiosurgery or with surgical resection plus postoperative fractionated radiotherapy. In the Gamma Knife group, 5 local recurrences and 36 new metastases occurred among 98 patients, which required secondary treatments with Gamma Knife, WBRT (n=12), or surgical resection (n=2). In the surgery group there were 53 recurrences requiring second treatments with surgery (n=2), Linac (n=21), local radiation therapy (n=3), and WBRT (n=1). All the resulting costs were compared. For the entire cohort, the median survival time was 14.0 months in the Gamma Knife group, compared to 10.2 months in the surgical group.²⁸

Apart from these clinical benefits, Gamma Knife treatment was also significantly more cost-effective compared to the surgical resection of brain metastases. Gamma Knife treatment for brain metastases was associated with a lower average cost (€9,964) than surgical resection (€11,647), Gamma Knife being significantly more effective in terms of LYS (life years saved) than surgery (1.53 LYS versus 1.08 LYS). When determined per individual patient and when all costs for potential recurrences or secondary brain metastases were taken into account, the final result of this study showed that Gamma Knife radiosurgery in the public German health system costs less than surgical resection, while increasing LYS by 0.45 years.²⁸

Summary

Current trends in European health economics are a decreasing number of hospital beds and shorter hospital stays, which can be assumed to result in higher priority for minimally invasive or outpatient-based treatments. The exponentially increasing use of Gamma Knife radiosurgery is one of the results of this general environment.

Due to a substantial proportion of fixed expenditures, the radiosurgical costs depend on the number of treated patients per unit, resulting in considerable variability of cost estimations in economic publications. The published direct costs for radiosurgery range, depending on the regional environment, from \$20,209 (US 1995) to €2,412 (Netherlands 2011). The extremely low reimbursement is only possible in the rare circumstances of public cost calculations, which are not based on a return on investment. Cost/benefit calculations should comprise direct and indirect costs, including capital and operating costs, staff, length of hospital stay, imaging, diagnostics, follow-up, costs of complications, and ancillary treatments. Factors such as procedural morbidity and even mortality will significantly influence the cost/benefit ratio. Indirect costs from a socioeconomic perspective comprise lost workdays and the need for rehabilitation. Reliable cost comparisons are highly complex due the multitude of these interdependent factors.

Surgical and radiosurgical indications are not always equivalent; however, in many indications radiosurgery has replaced the open surgical resection. In direct comparison with open surgery, Gamma Knife treatment requires lower direct, indirect, and ancillary costs. In uncomplicated AVM, surgical resection can offer some QALY advantage over radiosurgery due to its immediate curative effect, provided the surgical morbidity is very low. On the other hand, several analyses emphasize the cost effectiveness of Gamma Knife vs. surgery due to reduced treatment-associated morbidity in radiosurgery, particularly in the treatment of complex tumors such as acoustic neuroma and meningioma. The result is lower treatment-associated morbidity and shorter hospitalization. Radiosurgery has a positive socioeconomic impact due to a considerably lower number of lost workdays. When all the costs for potential later recurrences or secondary tumors were taken into account in the treatment of brain metastases, it was shown that Gamma Knife treatment increases LYS (life years saved), while being associated with lower total costs than surgical resection. When compared to the frequently employed very inexpensive but likewise frequently inefficient fractionated whole brain radiotherapy of brain metastases, it was shown that radiosurgery has a superior therapeutic effect, resulting in lower costs per year of median survival.

Cost analyses demonstrate that Gamma Knife radiosurgery has all the economic advantages of a minimally invasive method with reduced staff requirements, shorter hospitalization and less treatment-associated morbidity.

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