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Original Article

The efficacy of stereotactic radiosurgery in the management of Vestibular Schwannomas – a retrospective analysis

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Abstract

Vestibular Schwannomas (VS) are benign tumours arising from the neural sheath of the vestibular nerve, located near the auditory canal and cerebello-pontine angle adjacent to the brainstem making tumours "malignant by position". With high complication rates following surgery for tumour resection it is essential that alternative yet comparable management options such as Stereotactic Radiosurgery (SRS) be more fully evaluated in order to attain its efficacy and provide patients with alternative treatment modalities.

The aim of this study was to critically evaluate the treatment outcomes of patients treated with SRS for Vestibular Schwannomas at the Cromwell Hospital's Gamma Knife Centre between 1998 and 2002. To facilitate this, information regarding patient's clinical history and SRS treatment parameters was collated and analysed via departmental on-line systems.

In total the study provided a representative sample size of 74 patients with follow up data ranging from 6 months to 4 years post SRS (with a median of 12 months).

At the maximum point of follow up attained by each patient 43% had an overall smaller tumour volume than at the time of treatment whilst 18% demonstrated a volume increase and 39% remained unchanged. In total 67% demonstrated evidence of decreased central tumour contrast enhancement (necrosis). 27% of patients suffered some form of immediate complication post SRS, all of which had resolved within 6 months. No correlation was found between the severity of the complication, prescription dose and tumour volume.

Results are comparable with those from other published series highlighting a positive response from the tumour (decrease in volume) with few immediate complications, largely unchanged severity of symptoms post SRS and no negative impact on the patients quality of life. Although a number of significant papers have been published regarding the role of SRS in the management of VS there remains no definitive answer as to the best management option. Tumour control rates are comparable in both options and whilst both have their limitations, complication rates are generally much lower in the SRS group. Even so it is yet to be widely accepted as the treatment of choice in suitable cases. Nonetheless broadening the knowledge base with more research and education regarding the benefits of SRS will allow it to be promoted as a primary, contemporary treatment option in the management of VS.

Keywords

Stereotactic radiosurgery; gamma knife; stereotactic radiotherapy; vestibular schwannoma

INTRODUCTION

Brain tumours account for approximately 1.7% of cancers worldwide. Whether malignant or benign any tumour within the brain is considered a "space-occupying lesion" and must be carefully managed.[1] Conventional treatments include surgery, and radiotherapy, with cytotoxic chemotherapy being of little use due to the constraints of the blood-brain barrier.[2] Whichever treatment is

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preferred for tumour management has implications for the patient in terms of risks, recovery periods and side effects.

One group of tumours providing challenging management approaches are Vestibular Schwannomas (VS). Arising from the neural sheath of the vestibular nerve, they are benign in nature, but their location at the auditory canal and cerebello-pontine angle (CPA), adjacent to the brainstem makes these tumours "malignant by position".[3]

The history of treatment approaches for VS has been influenced by technological advances which impacted upon not only on the management of the disease but also the diagnosis and prognosis.[3] With the introduction and development of high-resolution volume acquisition magnetic resonance imaging (MRI), tumours can be detected earlier, before the onset of symptoms thus increasing the probability of control.[4,5,6]

One significant development in the management of VS is the role of Stereotactic Radiosurgery (SRS). The development of SRS over the past decade allows it to be offered as a reliable non-invasive strategy for a number of brain malformations and tumours.[7] Its aims are clear, to control the tumour growth whilst maintaining existing neurological functions. It is now gaining respect within the medical community as:

"A definitive alternative to microsurgery for patients with newly diagnosed, recurrent or residual benign tumours such as acoustic neuromas."[8]

LITERATURE APPRAISAL

The mainstay for treatment of VS has long been surgical resection, which has been significantly refined during the past 20 years. Results of surgical resection when performed by experienced surgical teams are excellent and have been significantly enhanced with the development of the operating microscope. However it is those patients treated by surgeons inexperienced in such technique which gives rise to concern.[9] In the hands of an experienced surgeon and with sophisticated anaesthesia and peri-operative care, mortality rates have been lowered to 1%. The most common complication being cerebral spinal fluid (CSF) leakage.[10] There is 95% likelihood of normal or near normal facial nerve function with a hearing preservation rate of 70% and less than a 0.3% recurrence rate.[3]

Even so, surgical morbidity and mortality rates are not insignificant. Many studies concern themselves with assessing the complications which arise mainly from injury to the nearby brainstem and cranial nerves. One assessment of published data reveals facial nerve continuity is lost in 7% of surgical patients and amongst the remaining 93% with anatomical preservation of the nerve post surgery, 45% exhibit new facial deficits.[11] Although facial and trigeminal nerve complications are a crucial factor, impacting upon patient quality of life, other surgical complications can occur. These include CSF fistulas in 15%, cerebellar/brainstem injury with permanent ataxia in 0.6%, meningitis in 3%, intra-cranial haemorrhage in 2%, other cranial neuropathies in 2%, hemiparesis in 1%, tetraparesis in 0.2% and death in 1%.[5,11]

These complications, although rare, pose definite problems and are important considerations for clinicians and VS sufferers. Can patients be spared having to undergo surgery, by the use of the less invasive treatment option of SRS, with comparable results and less associated risks?

An early study by Forster in 1996[12] was less than convincing. There was however, a high rate of evaluated cases not returning for follow up. This may explain the high failure rate seen in his series?.[13] Perhaps the limiting factor was itself the use of computed tomography (CT)? Kondziolka et al. (1998)[14] indicate that poor results in early papers may be related to the use of CT, and that planning radiation doses on the basis of CT scans compared to MRI is an unsatisfactory approach as the intra-canalicular portion of the tumour can not be well visualised, which implies a significant risk factor for induced hearing loss.

Although Forster's work has been superseded, his work was pivotal in promoting SRS, addressing the need for wider acceptance and further research to aid development of this treatment option. Subsequently, Kondziolka et al. published

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findings from the University of Pittsburgh in 1998. A change in trend was already apparent with the opening sentence:

"Stereotactic radiosurgery is the principle alternative to microsurgical resection for acoustic neuromas."

This study offered an impressive 98% control rate with normal facial function preserved in 79% of cases and a maintained pre-treatment hearing level in 51% of cases. For the first time, this study looked into the patients perspective and quality of life after SRS by assessing patient satisfaction via post treatment questionnaires. 92% of patients said SRS had met their expectations (although this was not comprehensively defined) and was found to be preferable in patients who had also undergone resection previously.[14]

Kondziolka's work added another perspective. Forster et al.[12] reserved SRS for patients who had failed surgery, residual or recurrence, a tumour in the only hearing ear, bilateral tumours, old age and those who refused surgery. This stringent patient selection criteria was employed as a result of lack of evidence regarding the outcomes of SRS, short and long-term complication rates, long-term tumour control, risk of radiation induced neoplasms and the risk of delayed microsurgery. Consequently SRS was not recommended as an alternative to surgery in healthy patients.[10] However, the work of Kondziolka et al. (1998)[14] allowed SRS to be performed on younger patients with results comparable to those found in older patients.

A significant development occured in 1998 when SRS was offered to all patients with VS regardless of age, surgical history or symptoms, the only limiting factor being tumour size.[14] Although this criteria is still employed by most radiosurgery departments, work by Spiegelmann et al. (2001)[5] raised concerns about using high doses of radiation to treat a benign condition, especially in young patients, arguing the theoretical possibilities and long-term complications of malignant transformation of the tumour.

Technological developments have prompted a continuation of research and appraisal of radiosurgical techniques. A significant step forward was research published by Prasad et al. in 2000.[13] This addressed all of the key topics surrounding the use of contemporary SRS. Results of treatment efficacy and functional outcomes were excellent including retained facial nerve function and integrity of the trigeminal nerve without neuralgia significantly impacting on quality of life.[20] Their protocol led to an impressive combination of a maximum of effect (tumour control) at a minimum cost (low morbidity). The authors clarified many issues frequently raised on temporary volume increase and the importance of loss of central contrast enhancement.[13] Furthermore, Vermeulen et al.'s results in 1998 [cited in 20] highlighted that good results and functional outcome can be achieved with protocols such as that developed by Prasad. The need for long-term follow up studies was mooted. It is recognised in a number of studies that there is a particular amount of unseen biological activity which can occur for certain periods in specific tumours. Therefore to accurately assess all VS patients after treatment we need to give these tumours adequate time to achieve a matured biological state.[13] Results from Foote et al. (2001)[11] found the average post-treatment interval to detection of tumour growth was 25 months, when considered, this should not come as much surprise as we are dealing with a benign, slow growing condition, however it does substantiate the need for long-term follow up.

Technological advances have allowed SRS techniques for VS to evolve, with significant improvement in treatment volume to tumour volume 3D conformality. Key drivers for this improvement have been the change to volumetric MRI stereotactic targeting and the routine use of multi-isocentre planning.[15,16] With particular reference to treatment for VS, the biggest impact on reducing complications has been refining prescription doses. Originally conceived to create functional lesions within physiological tracts or nuclei, SRS was designed to administer doses that caused liquefaction necrosis within the tumour volume (TV). Subsequent application of the technique for patients with intracranial tumours soon demonstrated that doses which led to tissue necrosis, also led to unacceptably high complication rates.[15] Generally radiosurgical doses are prescribed to the isodose covering the periphery of the tumour, with the aim of shaping the dose distribution so that the border of the target is

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enclosed by a surface dose between 50% and 70% of the maximum dose, reflecting the theory of combining a high dose within the target and a rapid fall off at its periphery.

Radiobiology indicates that tissue response to radiation is volume dependant. The largest fraction of a given volume is located at its periphery. If a small margin is added to the target volume this margin contributes significantly to the total volume that is irradiated to a high dose. For a given dose, the likelihood of side effects increases with the irradiated volume.

In the case of VS, early published studies gave tumour margin doses of 18–20 Gy and provided high cranial nerve neuropathies of around 18% [cited in 11]. Further experience with lower doses demonstrated that necrosis-producing doses were not necessary to inactivate neoplastic cells biologically or to achieve permanent growth control of benign tumours.[17] Thus marginal doses are now limited to between 10–14 Gy, dependant on various factors namely audiologically confirmed hearing levels on the affected side. Doses lower than 10 Gy have not proved effective in maintaining tumour control.[18] In general the available data suggests the incidence of tumour shrinkage was not significantly affected by the lower doses but it did eliminate all incidences of neuropathies.[5,14,19]

The vast majority of published research establishes SRS as a viable alternative to microsurgical resection for VS. It must be considered that due to rapid evolution of SRS procedures (i.e. prescribed dose, MR imaging and sophisticated planning software) it is problematic to compare published reports and draw definitive conclusions.[21]

METHODOLOGY

The aim of this study was to critically evaluate the treatment outcomes of patients treated with SRS for Vestibular Schwannomas at the Cromwell Hospital's Gamma Knife Centre between 1998 and 2002. For the purposes of this study a non-experimental design was adopted. All data required for analysis was available within departmental resources. However the relevant data had to be extracted, re-formatted and interpreted with the studies specific aim in mind.

Tumour volume definition

The TV was defined on saggital MR images transferred via the system network to the planning system (LGP). The radiosurgical target was defined and outlined by the gamma knife team consisting of a neuroradiologist, neurosurgeon and physicist, the same approach was employed for volumetric assessment at follow up. Treatment was carried out using standard Gamma Knife Radiosurgical procedures.

When assessing follow up images it becomes difficult to assess what is true volumetric change and what is just measurement error particularly when tumours are defined to the nearest cubic millimetre. For the purposes of this study a method defined by Karpinos et al. (2002)[22] was employed. Based on estimates of neuro-imaging and measurement error a change in the TV of at least 3.0 cubic millimetres (0.003 cubic centimetres (cc)) was required to consider any two tumour measurements "objectively different". If the change was less than 0.003 cc it was interpreted as inter-observer variability and therefore recorded as unchanged (UC).

Sample size and exclusion criteria

The sample was drawn from patients having received SRS for VS at the Cromwell Hospital's Gamma Knife Centre between 1998 and 2002. Following treatment all patients were invited to return after 6 months, for follow up MRI scan in stereotactic conditions. This was compared to initial pre-treatment scan to assess any change in TV, and to review the amount and density (if any) of decreased central contrast enhancement, indicating the presence of radiation induced necrosis.

Only patients who had attended a minimum of 1 follow up would be included within the study to gain an accurate representation of treatment data. Those patients who were yet to reach the first follow up presented no data to be analysed and would therefore give a false representation of attrition rates and no useful data would be gained by including such patients. However it was felt important that all available follow up information should be utilised regardless of whether is it 6 months or 4 years worth of data in order to assess the progression and response of the tumour.

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To provide a valid sample it was decided all patients who had attended at least one follow up (6 months post treatment) on or before the 1st September 2002 were to be included in the study, including those who have failed to attend for follow up as it is important to realise attrition rates. This defined the sample type selected as a cluster sample, since each member of the available population (after exclusion criteria were established) was selected and included in the study.

Data collection methods

All outcomes were measured for comparison to assess the effectiveness of treatment and attain some information regarding the behaviour and response of the tumour post SRS. When analysing the outcomes of treatment it must be remembered that VS is a benign tumour. The aim of treatment using SRS for these tumours is not to remove the tumour but to control its growth.[11] Therefore, success of treatment was measured by a reduction in the TV and any symptomatic control or resolution compared with levels attained pre-treatment. Any alteration in TV was assessed and analysed with comparison to the length of follow up.

The presence of any central necrosis (interpreted as decreased central contrast enhancement) detected on MRI was recorded. This information was compared to any change in the TV, at what stage of follow up it was detected and (if multiple follow up information was available) if there were any subsequent changes in the TV as a result, and finally, if there was evidence of necrosis at the initial follow up how this changed during the successive analysis. This information was then used to establish any relationship between necrosis and tumour shrinkage. Other treatment outcomes were assessed via analysis of symptoms suffered by the patient and their severity compared to pre-treatment levels, this was done by comparing results from audiology tests where available and clinical notes taken during the consultation.

RESULTS

Sample size

At the close of the study 108 patients with VS had received SRS at the Cromwell Hospital's Gamma Knife Centre. Of these, 93 were eligible to be included in the study having reached the first follow up period of 6 months post treatment, therefore a total of 86% of all patients treated for this condition were included in the study.

Of those patients eligible for inclusion in the study, 19 were lost to follow up giving an attrition rate of 20%, therefore the study provided a representative sample size of 74 patients (80% of those eligible for inclusion).

Treatment statistics

Various treatment statistics were collated:

- The range of tumour volumes (TV) treated were between 0.091–22.1 cubic centimetres (cc) giving an average TV of 3.15 cc and a median of 1.35 cc.
- The prescription doses (defined as that encompassing at least 90% of the TV) ranged from 10–16 Gy with the average being 12.5 Gy with a median of 12 Gy.
- Prescription Isodose lines (PI) ranged from the 40–65% with the median and mean isodose being the 50%.

Length of follow up

In total 74 patients had attended for follow up at some point following treatment varying from 6 months post SRS – 89% (66/74) to 4 years post SRS – 1% (1/74).

These results were then further split into the maximum follow up period attained by each patient which produced a median length of follow up of 12 months with an average of 14.1 months.

Figure 1 shows the percentage numbers of patients who attended for follow up. The grey area represents the total numbers of patient who attended at each stage whilst the black area highlights the maximum length of follow up attained by each patient. Therefore a high total attendance rate can be seen at the 6-month stage whilst over half of patients continued to attend for further later follow-ups. Figure 1 also highlights the median length of follow up (12 months) and a low overall attendance at the 18-month stage.

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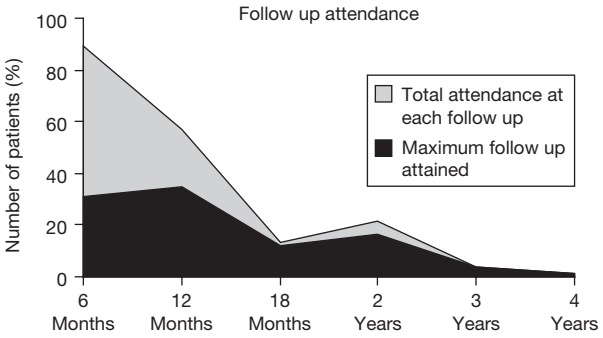

Figure 1.

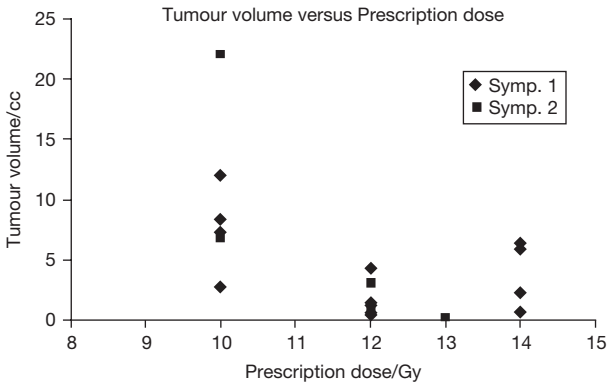

Figure 2.

Presenting signs and symptoms

Out of the 74 patients included in the study 97% (72/74) presented with affected hearing, of these 67% (48/72) were unilaterally deaf. Other more prevalent symptoms included: Tinnitus – 46% (34/74), Imbalance – 46% (34/74), Facial (7th) Nerve Neuropathy – 14% (10/74), Headaches – 5% (4/74).

Immediate complications

Defined as, complications arising as a direct result of treatment and occurring within the first two weeks following SRS. 27% (20/74) of patients suffered some form of immediate reaction or complication as a result of the treatment, some of the more serious included increased tinnitus (4/20), worsening of hearing (2/20) and ataxia (1/20).

By the time patients attended their first follow up (6 months post treatment) symptoms had significantly improved or resolved in every patient.

COMPLICATIONS VERSUS TUMOUR VOLUME

Of the 17 Patients who had immediate complications they were classified as:	
• Mild	71% (12/17)
• Moderate	29% (5/17)
• Severe	None
These were then compared to TV	
• Small	41% (7/17)
• Medium	18% (3/17)
• Large	41% (7/17)

Figure 2 represents the severity of symptoms suffered post SRS (Symp. 1-mild, Symp. 2-moderate) and the TV and prescription dose received by each patient. It shows no correlation between TV, prescription dose and the severity of the symptoms but highlights a more generalised distribution with the worst symptoms seen in patients with small or large TV receiving a low or average prescription dose.

Symptoms post SRS

At the time of follow up all patients were assessed and any change in presenting symptoms recorded, alongside the onset of any new ones. At every stage of follow up the majority of patients remained clinically unchanged. Figure 3 shows the number of patients suffering symptoms at each stage of follow up.

Figure 3 represents all symptoms suffered after SRS. It highlights the total number of patients suffering each symptom, separated into follow up stages. It demonstrates that overall the majority of patients symptoms remained clinically unchanged following SRS. Of those who did suffer symptoms post treatment the majority were seen early on in the follow up process generally at the 6 and 12-month stages, however, it is acknowledged a higher proportion of patients attended at these stages.

Tumour volumes

Overall, 73% (54/74) of patients showed some change in TV after SRS. However of the 20 who showed no evidence of volume change after

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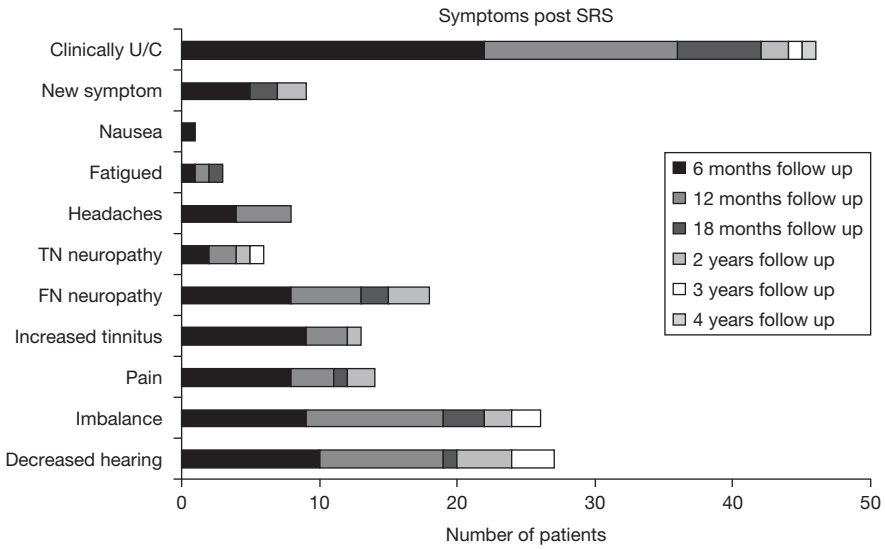

Figure 3.

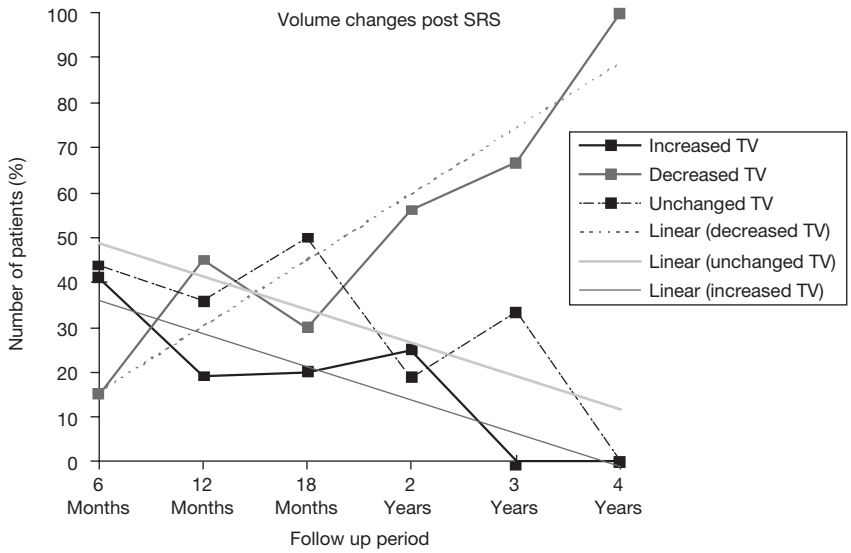

Figure 4.

treatment 11 had only reached the initial follow up period of 6 months.

When looking at the response of the tumours over the follow up periods they were placed into one of three categories for each period of follow up, increased, decreased or no change in TV. The most important results with respect of mapping tumour response were from the 6 and 12-month follow-ups as this was when the most significant TV changes occurred. Of those demonstrating a reduction in the overall TV, 5 remained larger than at time of treatment although a reduction had been seen following the initial increase at 6 months.

Figure 4 shows the trends in TV over the course of all follow-ups. It highlights a decrease in the TV after an initial increase at 6 months and shows the majority of patients who demonstrate a long follow up history exhibit an overall decrease in TV over time.

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VOLUME REDUCTION

Where TV had increased at the 6 months follow up stage volumes had started to decrease again subsequently in 16 patients (89%). Of these, 11 had returned to a volume less than or equal to that at the time of treatment by the 12 months follow up and 2 by the 2 years follow up. In the remaining 3 patients TV were still larger than that at time of treatment but had started to decrease after the initial period of increase at 6 months.

Necrosis

Results were assessed to evaluate the presence of necrosis at time of follow up, due to the information available this was only possible to assess at the 6 months follow up. Overall 67% (44/66) of patients who attended for 6 months follow up showed some evidence of reduced central contrast enhancement, interpreted as necrosis, irrespective of any change in TV.

Relating this to changes in TV observed at 6 months:

- 85% (23/27) of patients who demonstrated an increase in TV also showed evidence of central necrosis.
- 80% (8/10) of patients who demonstrated a decrease in TV also showed evidence of central necrosis.
- 45% (13/29) of patients who's TV remained unchanged also showed evidence of central necrosis.

DISCUSSION

Comparison of the treatment statistics with other published results from SRS studies show comparable control rates. Median follow up rates were comparable with the lowest seen in the series at 12 months, with a maximum data range of 4 years, conclusions from Flickinger et al.'s (2001)[4] showed the crucial phase for mapping volume changes to be in the first three years.

Reasonable tumour control rates of 92% were observed compared with a median over the SRS group of 95.8%, with very low comparable facial and trigeminal nerve neuropathies of 2.7% in both cases.

Interesting to note, is the change in trend of typical prescription doses since 1995 to 1998, which were a response to the high trigeminal and facial nerve complication rates previously observed. It has been widely accepted within the radiosurgical community; following early pioneering studies that using conventional doses of around 14 Gy indicated high complication and delayed neuropathy rates. Cranial nerve morbidities have improved over the last 5 years, with current literature suggesting a 6% neuropathy rate that can be directly ascribed to lower isodose prescriptions.[23] It is now accepted that doses of around 12 Gy provide adequate tumour control whilst significantly reducing risks to the patient. However studies also show that dose reduction from 12.5 Gy to 10 Gy were associated with a 6-fold greater incidence of tumour regrowth after SRS.[18] In general the available data suggests the incidence of tumour shrinkage was not significantly affected by the lower doses but it did eliminate all incidence of neuropathies.[5,14,19] Research from Foote et al. (2001)[11] analyzing risk factors of SRS, suggested a prescription dose of 12.5 Gy to the tumour margin resulted in the best combination of maximum tumour control and minimum complication rates (this did not seem to be effected by TV). Results from this study are comparable with this, showing an average prescription dose of 12.5 Gy and median of 12 Gy.

Length of follow up

The highest proportion of patients reached the 12 months stage, if we interpret this with the efficacy of the TV data in mind it indicates that any volumetric data analysis would be valid as a true representation of tumour response, after any initial volume increase due to radiation induced necrosis or oedema can be assessed. 16.2% of patients subsequently reached the 2-year follow up period, providing more data for analysis and interpretation allowing a more valid representation of tumour response. It must be remembered however that according to Foote et al. (2001), the average post treatment interval to detection of tumour growth is 25 months, this would suggest limited reliability of results from this study, however, as addressed previously median length of follow up is comparable with other similar published studies but it must be remembered when drawing

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conclusions there is a fundamental prerequisite for longer follow up assessment as data becomes available.[4,11,23]

Presenting signs and symptoms

Due to the anatomical position of VS in the cerebello-pontine angle the majority of patients present with symptoms related to pressure or damage of the 8th cranial nerve. Results from this study are consistent with this the most frequent symptoms suffered being hearing loss, tinnitus and imbalance. Overall 97.3% of patients presented with affected hearing, although it appears few patients actually had audiologically confirmed deafness 22.2% (16/72) this figure is not totally reliable. In most cases audiology tests were only performed in patients where, in the consultant's opinion the patient maintained *some* level of functional hearing. This was assessed during the pre-treatment consultation via clinical examination and asking the patient's perception of their hearing, actual numbers show 39.2% of patients were unilaterally deaf at time of presentation. It is essential to gain an accurate indication of hearing levels as ultimately it affects the prescription dose. If the patient maintains some useful hearing every effort would be made to maintain this and doses set accordingly. It is important to remember that VS are benign and therefore quality of life (QOL) after treatment is a crucial factor. As long as sufficient dose can be given to control tumour growth and stop it causing further problems it is unnecessary to deliver doses which will cause permanent irreversible damage to crucial structures such as the acoustic, facial and trigeminal nerves.

Other presenting signs and symptoms included neuropathy of the 5th and 7th (Facial and trigeminal) nerves with a 12.2% and 13.5% presentation respectively, which comes as no surprise given the anatomical location of the tumour in close proximity to these nerves. Vertigo and ataxia were also seen in a small number of patients, these symptoms are very rare and not conclusively documented in other studies therefore it is impossible to draw comparisons, however it is clear from more surgically orientated papers that such symptoms arise usually as a result of compression from mass effect associated with large tumours,[24] this can be substantiated in all cases as the smallest associated volume was 3.6 cc. Similarly in the two cases of patient presenting with hydrocephalus (HCP) both were as a result of mass effect again from large TV's, HCP is caused by the tumour obstructing cerebrospinal fluid (CSF) pathways or by a high CSF protein content impairing absorption of CSF.[25]

Tumour volumes

A large increase in TV was seen at 6 months, this was to be expected and can be confirmed throughout the literature as a typical tumour response. It is accepted that such increase is directly related to an early radiation response by the tumour. Early reports suggested doses that led to liquefaction necrosis within the tumour also led to unacceptably high complication rates [cited in 15]. Prasad et al.[13] addressed this phenomenon stating it was clear from their observations that the transient increase in TV represented an early change in response to radiation and although there is no clinico-pathological data to explain this, its reversible nature is perhaps an indicator that the increase represents some kind of turgidity in the appearance of the lesion. With this in mind it is essential to exercise diligence when assessing TV at 6 months. There was a significantly higher incidence of central non-enhancement in tumours that exhibited an initial increase in volume (85.2%) compared with those that did not (44.8%), these results are comparable with those seen in Prasad's study (75% and 46% respectively). If we assess trends, after the initial large volume increase at 6 months trend lines show a linear decrease in the rate of tumour growth whilst the highest proportion, across all subsequent time scales, showed a decrease in TV, results comparable with those from other studies.[13]

The important conclusion to be drawn from this is that the volume seen at 6 months shows a transient increase and should not be confused with tumour growth and consequently treatment failure which could warrant the patient undergoing unnecessary surgery. Any perceived volume increase is usually representative of swelling and not growth.[26,27] This was confirmed in the author's study, since for those patients demonstrating an initial volume increase, 88.9% subsequently demonstrated a reduction in TV with 68.8%

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having returned to the pre-treatment volume by the 12 months follow up. What is clear however is that the true significance of these changes still needs to be fully established, it may be that in the future better delineation and assessment could be made utilising Single Photon Emission Computerised Tomography (SPECT) or dynamic MR imaging in order to more fully understand aetio-pathogenesis.

In three cases TV continued to increase and patients required further treatment, one had surgical intervention as the TV was so large whilst the other two had repeat SRS. It is worth noting that in the patient requiring surgery, the previous SRS was not found to be a limiting factor or to affect the surgical removal of the tumour. Some studies have shown concern that previous irradiation from SRS can limit the viability of subsequent surgical intervention. In those who received second SRS an assessment was made of the prescription doses and PI from the first SRS in these two patients alongside the TV. No correlation could be found and therefore no conclusions drawn as to why the initial treatment failed to control tumour growth. Both underwent further SRS, at the close of study one had attended for the first follow up after the second treatment. Results from this indicated the TV remained unchanged however marked central non-enhancement was noted.

Assessing TV remains problematical, even after comparing results with those from other studies it remains unclear as exactly how to define and interpret findings, this is an area which the neurosurgical community needs to come to some consensus on. What is clear however is that as long as tumour growth is arrested, symptoms controlled and patients suffer no serious long-term complications as a result, then with respect to the treatment of this benign condition, this is a successful outcome.

Immediate complications

Following treatment there was a 27% immediate complication rate, defined as new symptoms occurring as a direct result of SRS within two weeks of treatment.[16] In patients treated with SRS, larger tumour size and a smaller number of isocentres used are associated with a higher rate of total hearing loss and facial and trigeminal neuropathy.[22] However results highlight that in this series there is little correlation between severity of symptoms encountered, prescription dose and TV. All symptoms were mild or moderate and mostly encountered in either the small or large tumour group. More symptoms were seen in patients receiving a low dose, which can be linked to TV, larger tumours receive lower marginal doses but produce a greater mass effect in comparison to smaller tumours. In patients who received the highest marginal doses they presented with the least severe symptoms, but this may be more attributable to TV rather that dose. The only conclusion that can be drawn from these results is that the incidence of immediate complications may be as proportional to dose as it is to TV.

Symptoms post SRS

More than 270,000 patients worldwide have been treated with the gamma knife to date,[28] but its entire side effect profile has never been fully defined. Generally authors consider the most significant and frequently observed complications associated with delayed neurological deficits. Hence there have been few reports focussing on immediate complications arising within the first few weeks of treatment. Acute side effects occurring in this period and subsequent longer term, (other than those associated with neurological deficits) are rarely discussed in studies of clinical outcome. Immediate symptoms post SRS are generally considered to be rare because many reports assessing the development of SRS related complications have focused on new, often delayed neurological deterioration.[29,30,31,32] In many cases the onus has been on neurological deficits however the author believes this to be misleading as other symptoms which contribute to patient morbidity have, until recently been overlooked.

Sutcliffe et al. described seizures occurring in 1/160 patients treated for Arteriovenous Malformations (AVM), "one or two" incidences of cellulitis occurring at the pin sites and some patients treated for posterior fossa lesions who experienced nausea and vomiting [cited in 33]. Forster et al. (1996)[12] noted a few of their patients suffered nausea and vomiting whilst Chakrabati et al. (1996)[33] observed headaches lasting 12–24 hours to be the most frequent complication. Chin

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et al. (2000)[34] documented complaints of headaches, nausea and vomiting were common but not consistently noted, the authors concluded that post SRS complications were rare. However in all studies authors do not attempt to attain conclusions for such complications. In the authors clinical experience an estimated 95% of all patients who undergo SRS complain of a headache within the first 5–10 minutes of the frame being removed after treatment, due to a release of the pressure exerted on the bones of the skull. This complication is transient usually settling within 24 hours however it must not be overlooked as a significant side effect given the number of patients who experience it.

Results highlight that the majority of patients remained clinically unchanged post treatment. Of those who did display some increase in their symptoms most were related to nerve neuropathy i.e. imbalance, further decrease in hearing, increased tinnitus, pain, FN and TN neuropathy. Delayed neuropathy is defined as the commonest post SRS complication with rates being well documented as generally relating directly to prescription doses, however results from this study are considerably lower than those in similar studies. Reasons for this are undoubtedly due to prescription doses and MR delineation of the target.[4,5]

SRS also has the advantage which comes from standardisation, applicability in a wide range of healthcare environments, a requirement for less training than more variable methods and the ability to compare results from different centres. This standardisation means that data regarding SRS is reproducible, results from different centres worldwide can be compared and experience of existing centres can be easily transferred to new centres. In contrast differences between various Linac designs make it difficult to standardise clinical results.[35] We must remember that SRS is an attractive yet unusual treatment modality in that it offers clinical outcomes comparable with, if not better than current alternatives, lower costs per treatment than current spending and overwhelming advantages in terms of patient acceptability.

Conclusion

Over the past decade there have been considerable advances in the management of brain tumours. Patients no longer have to endure the high risk factors associated with invasive surgery but instead have alternative options with comparable results. Although SRS is perceived as being a new option it is in fact the advances in diagnostic imaging and computer software that have allowed it to emerge as a cutting edge treatment approach. Although a great deal of research has been published promoting SRS and highlighting it as the treatment of choice in certain pathologies such as AVM's, in the case of VS there still remains much debate as to its efficacy. Studies such as this are crucial in broadening the knowledge base not only for consultants but also for patients whom in today's society are more aware of the options regarding their disease management. Given the need to extend the knowledge base in order to standardise the management of VS it is essential studies such as this are performed and results utilised as the validity of *all* results irrespective of the sample size must not be underestimated.

Ultimately, the efficacy of SRS in the management of VS is clear and cannot be disputed given the consistency of published results, it should be regarded as the primary contemporary management approach in all patients with small or medium sized tumours However, whichever treatment approach is adopted it is essential it is done solely with the best intention for each individual patient.

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