Acta Neurochir Suppl (2008) 101: 163–168

Printed in Austria

Radiosurgery from the brain to the spine: 20 years experience

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Summary

Introduction. Radiosurgery evolved from brain to spine. Mechanical and computer advances in linear accelerator (LINAC) radiosurgery apply precise single/fractional stereotactic radiation to multiple pathologies.

Methods. During a 10-year span the senior author used proton-beam radiosurgery in over 300 lesions, followed by gamma-knife, adapted and dedicated LINACS, including cyber-knife, in another 700 patients. The last 10 years, experience was accumulated with the Novalis in over 3,000 patients. Novalis uses a beam-shaper in a high-speed delivery LINAC. It operates using conventional circular arc, conformal static beam, dynamic conformal or intensity modulated modes. Patients treated with Novalis at the UCLA since 1997 were evaluated regarding effectiveness, complications and failure. These results were compared with previous 1997 data.

Results. Over 4,000 patients with trigeminal neuralgia/intractable pain, arteriovenous malformations/angiomas, metastases, ependymomas, gliomas, meningiomas hemangiopericytomas, schwannomas, adenomas, hemangioblastomas, and chordoma were treated. Spinal lesions were treated with frameless stereotaxis and on-line precision checks. Treatment was expeditious, comfortable and with reduced complications. Success is similar or superior to published data. Reduced treatment time of complex lesions and highly homogeneous dose compares favorably to other radiosurgery.

Conclusions. The senior author's experience validates the novel shaped-beam approach. Long-term follow-up supports safety and effectiveness and capability to treat brain and spine.

Keywords: Proton beam; linear accelerator; gamma-knife; radiosurgery; spine.

Introduction

During a span of 20 years, starting in 1986, the senior author had the opportunity to work and observe the development of several generations of stereotactic radiosurgery devices. Initially using the Proton Beam at the Harvard Cyclotron, the senior author had the opportunity to adapt modern imaging, MRI and CT scan to stereotactic radiosurgery. Largely dedicated to the treatment of arteriovenous malformations and pituitary adenomas, approximately 300 patients were treated per year. The concepts of on line imaging confirmation and fusion were present in the Proton Beam stereotactic room serving as the bases to the modern stereotactic radiosurgery devices and planning tools [3].

The Gamma Unit, already present at the University of California since 1982, had shown the importance of Radiosurgery worldwide with the units in Stockholm, Buenos Aires and Sheffield. It gained greater popularity with the work of the stereotactic group at the University of Pittsburgh starting in 1987. After experiencing radiosurgery with the Linear Accelerator using the relocatable Laitinen's stereotactic device at the University of Umea in 1988 and 1989 [20], it became clear to the author that the versatility of linear accelerators would have major impact in the applications of stereotactic radiosurgery, mostly with the possibility to add stereotactic radiotherapy [6] and spinal radiosurgery [8]. At the University of California the author used initially the gamma unit and further adapted linear accelerators to radiosurgery.

Methods

One thousand patients treated during the first 10 years of the author's experience using proton beam radiation in over 300 lesions, followed by gamma-knife [36], adapted linear accelerators to radiosurgery including cyberknife [1] and dedicated linear accelerators in another 700 patients comprise the first group of patients. This experience is compared with the last 10 years data accumulated with shaped beam stereotactic radiation throughout the nervous system in over 3000 patients.

Currently a beam shaper device mounted permanently to a high speed radiation delivery LINAC (800 monitor units) coupled with frameless stereotactic navigation system and on line imaging verification of target

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is used at UCLA (Novalis, BrainLab Heimstetten, Germany). This system has been described previously [35]. Patients treated at the University of California Los Angeles since 1997 were evaluated regarding effectiveness, development of radiosurgery complications and early failure of treatment. These results were analyzed in comparison with previous data of the same author. Technical aspects of proton beam, adapted, dedicated and shaped beam linear accelerator radiosurgery and stereotactic radiotherapy, as well as robotic linear accelerator radiosurgery have been extensive reported by the author and his group [1, 5, 8, 16, 19, 25, 28–30, 32, 34, 35, 38].

Results

Over 4000 patients were treated, including over 200 functional cases of trigeminal neuralgia, intractable pain, and areteriovenous malformations, cavernous angiomas, metastases, ependymomas, gliomas, meningiomas, hemangiopericytomas, schwannomas, pituitary adenomas, hemangioblastomas, chondrosarcoma and cordomas.

Demonstration of the treatment plan using state of the art imaging and target location is presented in Fig. 1. The 5 mm collimator isocenter is currently placed at the root entry zone of the trigeminal nerve affected with the 50% isodose line touching the surface of the brainstem. The dose is 90 Gy at 100%, i.e., maximal dose and the 45 Gy reaching the surface of the brainstem [18].

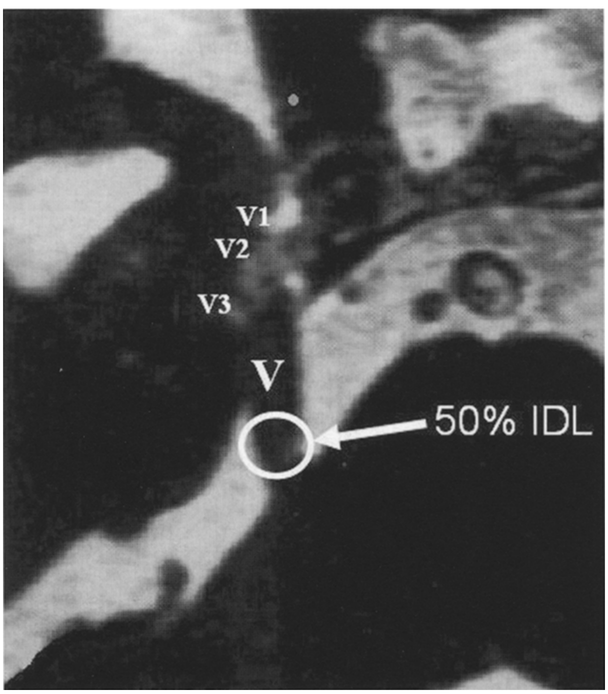

Fig. 1. Visualization of the trigeminal complex with magnetic resonance imaging using constructive interference steady state (CISS). Notice the target location at the root entry zone. The 50% isodose line touches the brainstem as demonstrated by the *arrow*. The dose use is 90 Gy to the target point, not to the volume demonstrated. 45 Gy touches the surface of the brainstem

Sphenopalatine ganglion is targeted for complex regional facial pain and cluster headache using the same dose prescription and collimator [12]. Functional targets in the brain such as thalamotomy [15] and cingulotomy are treated with 140 Gy, again using the 5 mm collimator, although the 3 mm collimator has also been used, making discrete and precise lesion [7].

Small arteriovenous malformations are treated with conformal single isocenter, homogeneous dose distribution and prescription with the 90% isodose line in the periphery of the lesion. Spetzler and Martin classification correlates well with the success rate of radiosurgery for this lesions, Grade 2 reaches 100% response while the Grade III reaches 60%. All Grade I AVMs are treated with surgery at UCLA [10]. Grade IV and Grade V AVMs reach 30% response rate, while VI reaches 60% [26]. The use of shaped beam radiosurgery reduced the complication rate from 5% [27] to transient complication of 2.5% [26]. Combined embolization is used in a trial of decrease AVM volume [14], however the main objective of embolization has been to treat arteriovenous fistulas present in the nidus, as well associated aneurysms. Currently stereotactic radiotherapy is used to decrease the volume of a large AVM, grade IV and V to again treat after a follow up of 3 years with radiosurgery. The pilot data of this approach shows a decrease in volume of giant AVMs of a mean of 72%, ($n = 20$). Figure 2 shows such an AVM that was treated with the protocol of 6 fractions of 5 Gy and stereotactic radiosurgery with 15 Gy at the 4 year follow up.

Initially as adjuvant therapy for skull base meningiomas [4], radiosurgery and stereotactic radiotherapy evolved as the techniques of choice in selected meningiomas locations [28]. Acoustic neuroma radiosurgery evolved from single dose only to small tumors to a trial a hearing preservation with stereotactic radiotherapy with a scheme of 2 Gy in 26 fractions. This approach has allowed preservation of 93% of useful hearing with a follow up of 3 years. The size decrease and absence of growth is observed for 100% of the tumors treated. Therefore the freedom of surgery after stereotactic radiotherapy has been 100%. Facial nerve deficit is less than 1% at this time [32]. The evolution of treatment was to bring maximal function preservation with maximal control rate. Single dose radiation is still used in patients who have lost hearing at the time of diagnosis, as with single dose of 12 Gy preservation of useful hearing was 60% in our hands.

Pituitary adenomas are approached first surgically, stereotactic radiosurgery is always offered when the op-

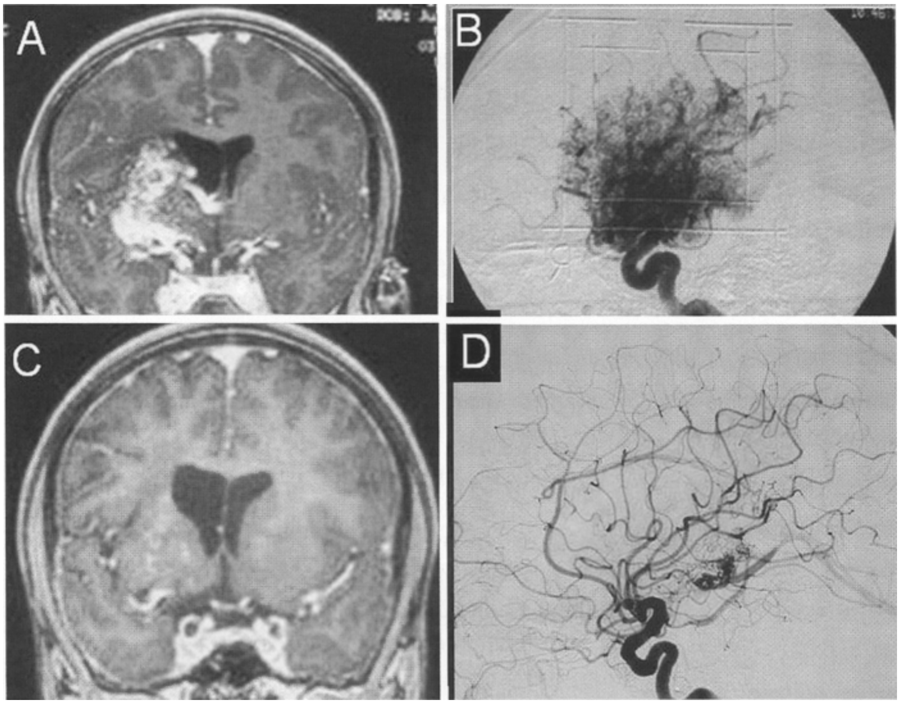

Fig. 2. (A) T1 Magnetic resonance image with gadolinium enhancement showing the giant basal ganglia AVM before stereotactic radiotherapy. (B) Lateral cerebral angiogram showing the lesion at the time of the treatment (6 Gy in 5 consecutive fractions). (C and D) Show the 4 year follow up, time of the radiosurgery of 15 Gy

tic apparatus is away from the tumor, at least 3 mm distance. Single dose is always preferred when hormonal burden is present. Stereotactic radiotherapy is offered when the optic apparatus is involved in non secreting tumors. The crude control rate of non secreting tumor with stereotactic radiotherapy has been 100% [30]. Craniopharyngiomas reached a three-year actuarial survival rates free of solid tumor growth or cyst enlargement of 94% and 81%, respectively [29]. Follow up as long as 9 years have shown that the cyst can recur even at this long term follow-up (Fig. 3).

Chordomas are treated with stereotactic radiotherapy to bring the dose to 72 Gy in fractions. Single dose is used with small residual and for boost when possible after stereotactic radiotherapy. Moderate length follow up has shown a control rate of 100 [25]. At longer follow-up (unpublished data) the control rate has held at 72%.

Since 1990 the preferred management of intraparenchimal matastases has been Radiosurgery. The presence of less than four lesions and no mass effect calls for radiosurgery. Innumerous lesions or lesion reaching the

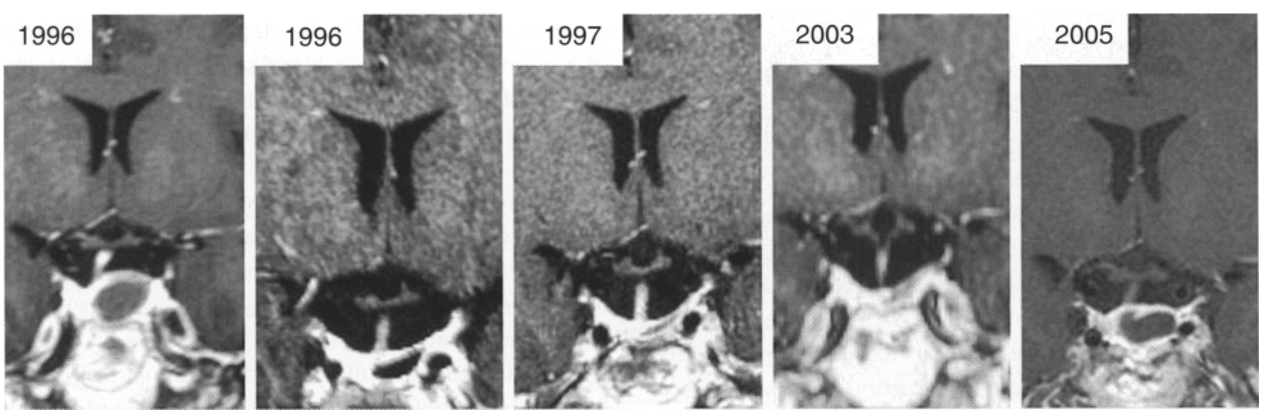

Fig. 3. Thirty six-year-old gentleman, with visual decline and headaches. Cystic craniopharyngioma recurred 1 year after transphenoidal complete removal. A stereotactic transphenoidal drainage of the cyst was followed by radiosurgery in 1996 (16 Gy to 70% isodoseline). Notice the control of the cyst for 9 years, when it recurred. Stereotactic radiotherapy was performed in 2005 (1.8 Gy to 90% isodose line, 28 fractions to a total of 50.40 Gy). The cyst has decreased in size and continues under control

cerebral spinal fluid are first managed with whole brain radiation therapy (WBRT), followed by imaging surveillance every three months. Radiosurgery is offered in case of new lesions or recurrence. This approach has avoided WBRT in 70% of the patients assuring better quality of life [2].

Low grade Gliomas are managed first with observation and SRT for cases with diffuse lesions or involving the optic apparatus. Discrete lesions are treated with SRS if possible. High grade Gliomas are preferably treated with regional conventional radiation therapy after a maximal resection. Stereotactic radiation is offered as a boost in selected cases [33]. Spinal lesions were treated with frameless stereotaxis and on line precision checks [8].

Discussion

Radiosurgery became an important addition on the armamentarium against trigeminal neuralgia [14]. Albeit powerful, it is the least invasive of the techniques [18, 19]. Using the protocol described above, 95% of the patients enjoy improvement of pain attacks. Recurrence is similar to the other techniques available, and a second treatment is possible, either with radiosurgery or any of the other techniques. Radiosurgery has the disadvantage of a latency period for pain response; therefore in cases of severe crises, the other techniques are preferred by our group [19]. Less successful applications of radiosurgery to control pain include sphenopalatine ganglinectomy [12], cingulotomy [13] and thalamotomy [15].

Epilepsy focus can be controlled by LINAC radiosurgery. Treatment of gelastic seizures caused by hypothalamic hamartomas has been successful to bring patients to a control at the level of Engle class II [31]. The senior author has a single experience on the treatment of left mesial temporal lobe seizure using the shaped beam approach with a dose of 17 Gy prescribed to the 90% IDL, 7cc volume. This patient had complete control of seizures, however need to use steroids for o period of 3 months due to radiation induced edema.

When possible, AVMs are managed with single dose application. Lesions larger than 5 cm in their largest diameter are managed in steps. Embolization is highly indicated in cases harboring large fistulas and aneurysms. These large fistulas do not respond appropriately to radiosurgery, and unsecured aneurysms pose high risk of bleeding.. The recanalization rate after embolization has been 9% in our earlier experience [27]. Therefore too early SRS following embolization may lead to failure to irradiate the recurrent portion of the AVM.

The acoustic neuroma treatment protocol evolved from single dose through hypofractionation schemes of 3 and 5 fractions. It was settled for 26 fractions of 2 Gy because of the outstanding results being observed with this protocol [11, 32]. Using 3 fractions of 7 Gy it was observed tumor swelling with need of steroid therapy. The scheme of 5 fractions led to the same hearing preservation of single dose when using from 12 to 14 Gy. Currently, the single dose of 12 Gy is used acoustic neuromas when there is no hearing to preserve.

Meningiomas involving the optic apparatus or with compression of the brainstem are treated with surgical decompression if possible, followed by either stereotactic radiosurgery or stereotactic radiotherapy. Deficits evoked by surgery are observed to resolution or stabilization to avoid a second insult to the structure in recovery. After surgery, depending on the meningiomas WHO classification [23], radiosurgery is deferred until confirmation of tumor recurrence. Patients are followed with imaging study in six-month intervals. When needed, the SRS or SRT choice for treatment depends on the need to avoid damage of structures involved by the tumor.

Radiosurgery took leading role on the management of metastases in our institution and many other advanced cancer centers. Our recent experience, currently under submission for publication by Ford *et al.* shows that when up to two intracranial lesions are present at the time of brain involvement, SRS offers statistically significant control rate and better quality of life than WBRT. Beyond two lesions significance was not found and WBRT must be entertained. Surgery should also be offered when possible for symptomatic lesions.

Gliomas either low or high grade are preferably managed by surgery, stereotactic radiation takes only an adjuvant role. Since focal radiation tends to lead to imaging changes of difficult interpretation when modern techniques are used, such as MRI, MRS or PET [17], we reserve stereotactic radiation only in the recurrent setting. This allows for better interpretation of results obtained with more promising clinical trials for these tumors, such as immunotherapy and chemotherapy.

The reduced time of treatment of complex radiosurgical lesions and the highly homogeneous dose to the lesion volume compares favorably to other radiosurgical techniques available and allow the choice of single, hypofractionation or full fractionated schemes. This provided increased effectiveness and decreased side effects, as demonstrated on the management of acoustic neuromas, cavernous sinus meningiomas and pituitary adenomas [28, 30, 32]. This experience has been transferred to spinal radiosurgery where we have observed crude 100% control of benign lesions and 83% of malignant lesions using 12 Gy single dose. Using this dose, no radiation induced myelopathy has been observed [8].

Experiment work

Strategies of treatment and new applications have been based on animal experimentation including for functional radiosurgery [7, 37], vascular radiosurgery [9, 21, 22] and spinal radiosurgery [24].

Acknowledgments

The author acknowledges the participation of his current stereotactic radiation team as co-authors and previous team members in the reference list. Retrospective data evaluation has been permitted by the institutional review board.

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