EDITORIAL

Stereotactic Radiosurgery

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Stereotactic radiosurgery represents a non-invasive method of precisely delivering a single large fraction of radiation to an intracranial target. This technique was initially developed by Leksell and colleagues in the early 1950's at the Karolinska Institute in Stockholm with an orthovoltage radiation source.[1] Since then three different methods of radiosurgery have been developed utilizing modern linear accelerators, cobalt sources (Gamma Knife), and charged particles (protons and helium ions).

Initially this technique was primarily intended for use in functional brain surgery for the destruction of deep fibre tracts or nuclei, but soon was used for unresectable arteriovenous malformations (AVM), acoustic schwannomas in elderly patients, and pituitary adenomas. In the last ten years there has been a proliferation of linear accelerator and Gamma Knife radiosurgery centres, and the technique is being increasingly utilized in the management of patients with gliomas, brain metastases, meningiomas, and other intracranial tumours in addition to the above mentioned conditions. This issue of the Journal contains three articles on linear accelerator based radiosurgery in patients with AVM and gliomas.

Young and her colleagues[2] from the Toronto-Sunnybrook Regional Cancer Centre report on their experience with the use of radiosurgery for the management of their first 50 patients with AVM with a minimum follow-up of 3 years. They have carefully documented their patient selection criteria, AVM size and location, and technique and dose of radiosurgery. The patient follow-up imaging and outcome are well described. Of note is the fact that their team is comprised of neurosurgeons, neuroradiologists, radiation oncologists and physicists amongst whom exists expertise in the microsurgical resection, embolization, and radiosurgical ablation of AVMs, a critical issue in the proper management of this patient population.

One of the major thrusts of this article is the discussion of the quoted obliteration rates reported in the literature. Young and colleagues[2] have a higher rate of angiographic follow-up (39 of 50 patients) than most reports in the literature, and demonstrate the significant variability of obliteration rates from other centres when the denominator includes or excludes patients without angiographic follow-up. This point has been previously stated for the literature on AVM by Mehta,[3] but the article by Young[2] has explicitly demonstrated the potential variations in obliteration rate and reminds us all that one must always exercise caution in the interpretation of reports of efficacy of any technology when the denominator does not include all patients having received the therapy under discussion.[3]

The other issue that arises from their report is the fact that approximately 30-40% of patients (depending on the denominator used) did not experience complete obliteration of their AVM in their series. In an elegant report from Pittsburgh, Pollack et al. reported on their experience with a second radiosurgical procedure on 45 patients with AVMs and retrospectively tried to assess possible reasons for the failure of the first radiosurgical procedure.[4] They found that incomplete angiographic definition of the nidus was the most frequent factor associated with failed radiosurgery (26 patients), usually due to inadequate appreciation of the 3 dimensional shape of the AVM based solely on orthogonal views at angiography. Most radiosurgical centres now incorporate either CT or MRI examinations or both in the target definition for their radiosurgical procedures. This issue does not appear to have been a concern in the current report by Young et al.,[2] as all 50 patients did undergo an enhanced CT scan of the brain in addition to angiography on the day of their radiosurgery. An inadequate dose of radiosurgery may be a contributing factor in their report, as there was a trend towards higher obliteration rates with the 20 Gray (Gy) cohort of patients (18/31) than the 15 Gy cohort (6/16), but small numbers of patients with variable rates of angiographic follow-up make this assessment difficult. While other authors have shown a correlation between increasing AVM diameter and decreasing obliteration rates, this small study did not demonstrate this relationship, in part because dose was meant to be 20 Gy for all patients and was reduced to 15 Gy by proximity to critical normal structures and not by size of the AVM.[5-8]

One novel approach to trying to improve the results of radiosurgery in the management of larger AVMs involves the use of staged radiosurgical procedures to portions of the AVM (volume staging) with higher doses with an interval of 3-6 months between procedures.[9] An alternative approach would be to fractionate the dose by treating the entire larger AVM with a few lower single doses, but the optimum number and size of fractions remain to be determined.

The second article in this issue of the Journal relates to the development of a predictive index of AVM obliteration by Schwartz and colleagues.[10] The cohorts of patients consist of 42 patients treated on a linear accelerator in Toronto and 394 patients treated on a Gamma Knife unit in Sheffield, England. The Obliteration Prediction Index (OPI) is equal to the marginal dose in Gy delivered to the AVM divided by the largest AVM diameter in centimetres. The mathematical exponential function describing the probability of obliteration relative to the OPI was developed on the Toronto cohort of patients and then applied to the Sheffield patients. There was an excellent fitting of the two curves from the different cohorts of patients which suggests that the OPI may be a useful adjunct in the prediction of probability of obliteration of a particular AVM in an individual patient. The authors intend to approach other radiosurgery centres to test this predictive model on their data.

This mathematical function has been generated empirically from limited patient data at essentially 3 dose levels (predominantly 15, 20, and 25 Gy) but provides a possible guide to the use of other dosages in individual cases. If this model is validated on data sets from other radiosurgical centres, then it would represent a valuable contribution to dose volume issues in the management of AVMs. This model confirms the known fact that lower radiosurgical doses and larger AVMs are associated with a lesser probability of obliteration with single fraction radiosurgical procedures.[5-8] The authors suggest that when assessing individual patients by this mathematical function, a patient with a low probability should either have the dose increased within known safety limits or the procedure abandoned and other modes of therapy be reconsidered. We would like to suggest that in patients in whom there is a low likelihood of obliteration and for whom the risks of alternative approaches remain high, that the OPI might represent one method of identifying a patient population in whom innovative methods of delivering radiosurgery might be appropriately investigated. These methods could include volume staging as suggested by the Pittsburgh group, or the use of a limited number of single fractions to the whole AVM.[9]

The third report on radiosurgery in this Journal issue comes from Shenouda and colleagues[11] in Montreal detailing a phase I trial of an initial 20 Gy fraction delivered stereotactically followed by an accelerated course of external beam radiation therapy delivering 60 Gy in 30 fractions in 4 weeks in 14 patients with glioblastoma. They report a median survival of 40 weeks, and possible significant toxicity in 2 patients. There certainly does not appear to be any benefit from this combination of accelerated external irradiation and the addition of a radiosurgical boost, but the small number of patients in this study prevents us from drawing any definite conclusions. Because of the inability to control the primary tumour, efforts in improving outcome in glioblastoma over the last few decades have been geared to increasing the intensity of treatment to the primary.[12] Brachytherapy as a means of increasing dose to the primary has resulted in at best in a modest improvement in median survival of 3 months as demonstrated in the Brain Tumour Cooperative Group and University of Toronto randomized study.[13,14] Currently brachytherapy is being replaced by radiosurgery as the preferred method of increasing dose to the primary tumour, and despite encouraging results from single institution series, it will remain to be seen whether radiosurgical boosts will contribute to improved survival in glioblastoma in the current randomized RTOG 9305 study.[15,16]

Stereotactically focused radiation, so-called radiosurgery, is a powerful and exciting adjuvant or alternative therapy for the treatment of difficult focal brain lesions such as AVMs and benign tumours (e.g., acoustic schwannomas, meningiomas) and certain malignant intra-axial tumours (notably metastases). There are numerous unanswered questions regarding the application of this exciting modality such as: 1) the relative efficacy of linear accelerator-based radiosurgery and Gamma Knife radiosurgery, the answer to which must not be based on emotional and political arguments, but on scientific examination of carefully collected data; 2) the role of radiosurgery in the treatment of malignant gliomas; 3) the optimal dose and fractionation regimes for various brain lesions; and 4) the understanding of the true long-term disease control rates and the long-term toxicity of this modality. Caution must be exercised in the interpretation of numerous one-armed and non-randomized two-armed studies comparing radiosurgery to other modalities.[17] Similar caution must be exercised in selecting patients for treatment with radiosurgery. Whenever a powerful instrument like this becomes widely available, the medical profession is often guilty of letting adherence to rigorous scientific principles lag behind the technological innovation. Currently, outstanding clinical and laboratory research is being done in the field by a number of thoughtful and careful investigators and many unresolved issues in the use of radiosurgery will be clarified within the next decade.

N.J. Laperriere and M. Bernstein
Toronto, Ontario

References:

1. Leksell L. The stereotaxic method and radiosurgery of the brain. Acta Chir Scand 1951; 102: 316-319.
2. Young C, Summerfield R, Schwartz M, O'Brien P, Ramani R. Radiosurgery for arteriovenous malformations: The University of Toronto Experience. Can J Neurol Sci 1997; 24: 99-105.
3. Mehta M. The physical, biologic, and clinical basis of radiosurgery. Current Problems in Cancer 1995; 19: 265-332.
4. Pollock BE, Kondziolka D, Lunsford LD, Bissonette D, Flickinger JC. Repeat stereotactic radiosurgery of arteriovenous malformations: Factors associated with incomplete obliteration. Neurosurgery 1996; 38: 318-324.
5. Engenhart R, Wowra B, Debus J, et al. The role of high-dose, single-fraction irradiation in small and large intracranial arteriovenous malformations. International Journal of Radiation Oncology, Biology, Physics 1994; 30: 521-529.
6. Fabrikant JI, Levy RP, Steinberg GK, et al. Charged-particle radiosurgery for intracranial vascular malformations. Neurosurgery Clinics of North America 1992; 3: 99-139.
7. Friedman WA, Bova FJ, Mendenhall WM. Linear accelerator radiosurgery for arteriovenous malformations: the relationship of size to outcome [see comments]. Journal of Neurosurgery 1995; 82: 180-189.
8. Flickinger JC, Lunsford LD, Kondziolka D. Dose prescription and dose-volume effects in radiosurgery. [Review]. Neurosurgery Clinics of North America 1992; 3: 51-59.
9. Lunsford LD. Stereotactic radiosurgical procedures for arteriovenous malformations of the brain [editorial; comment]. Mayo Clinic Proceedings 1995; 70: 305-307.
10. Schwartz M, Sixel K, Young C, et al. Prediction of obliteration of arteriovenous malformations after radiosurgery: The obliteration prediction index (OPI). Can J Neurol Sci 1997; 24: 106-109.
11. Shenouda G, Souhami L, Podgorsak EB, et al. Stereotactic radiosurgery and external beam accelerated radiotherapy for patients with glioblastoma multiforme: A phase I trial. Can J Neurol Sci 1997; 24: 110-115.
12. Laperriere NJ, Bernstein M. Radiotherapy for brain tumors. Cancer Bull 1993; 45: 337-345.
13. Green SB, Shapiro WR, Burger PC, et al. A randomized trial of interstitial radiotherapy boost for newly diagnosed malignant glioma. Brain Tumor Trial Cooperative Group Trial 8701. Proc Am Soc Clin Oncol 1994; 13: 174-170 (Abstract).
14. Bernstein M, Laperriere N, Glen J, et al. Brachytherapy for malignant glioma: Results of a prospective randomized study. Can J Neurol Sci 1997; 24: S21, Suppl. 1. (Abstract).
15. Sarkaria JN, Mehta MP, Loeffler JS, et al. Radiosurgery in the initial management of malignant gliomas: survival comparison with the RTOG recursive partitioning analysis. Radiation Therapy Oncology Group. International Journal of Radiation Oncology, Biology, Physics 1995; 32: 931-941.
16. Mehta MP, Masciopinto J, Rozental J, et al. Stereotactic radiosurgery for glioblastoma multiforme: report of a prospective study evaluating prognostic factors and analyzing long-term survival advantage [see comments]. International Journal of Radiation Oncology, Biology, Physics 1994; 30: 541-549.
17. Shrieve DC, Alexander E, Wen PY, et al. Comparison of stereotactic radiosurgery and brachytherapy in the treatment of recurrent glioblastoma multiforme. Neurosurgery 1995; 36: 275-282.

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