lifetime dose was over 2000 mg. It would be of interest, and reassuring, to know whether patients using a spacer device had a lower incidence of side effects. Spacer devices used with pressurised metered dose inhalers reduce oropharyngeal deposition of aerosolised steroids,<sup>5</sup> and hence the total body dose, without affecting the dose delivered to the airways. Their use has been documented to reduce hypothalamic-pituitary axis suppression by beclomethasone dipropionate,<sup>6</sup> and the British asthma guidelines recommend their use for the delivery of inhaled steroids.

Without information on the likely dose of drug inhaled, the results of clinical trials may also be misinterpreted.7 If more than one type of nebuliser or spacer is used in a trial the results should not be pooled as patients will probably have received different doses. The practice of subjecting patients to the risks and inconvenience of a clinical trial without taking the confounding effect of different drug delivery devices into account should be questioned. Similarly, regulatory authorities should review the information required of the manufacturers of drugs and drug delivery devices about the delivery of inhaled steroids. This may help in interpreting trial data for therapeutic effect and possible side effects. Advisory bodies on asthma management may also be able to give more informed information to both prescribers and patients.

Although significant side effects are apparently rare in users of low dose inhaled steroids, information on the dose of drug inhaled is of therapeutic importance. Patients are being prescribed inhaled steroids at younger ages, and lifetime doses may greatly exceed those reported in the current literature. Current advice remains that the dose of inhaled steroid, whatever the delivery device, should be titrated to the lowest dose at which effective control of asthma is maintained.

Christopher O'Callaghan Senior lecturer in child health Peter Barry Lecturer in child health

Department of Child Health, Leicester Royal Infirmary, Leicester LE2 7LX

- British Thoracic Society. The British guidelines on asthma management: 1995 review and position statement. *Thorax* 1997;52 (suppl 1):S1-24.
- 2 Committee on Safety of Medicines. Focus on corticosteroids. Current Problems in Pharmacovigilance: 1998:24:5-10.
- 3 O'Callaghan C. Particle size of beclomethasone dipropionate produced by two nebulisers and two spacing devices. *Thorax* 1990;45:109-11.
- 4 Cumming RG, Mitchell P, Leeder SR. Use of inhaled corticosteroids and the risk of cataract. N Engl J Med 1997;337:8-14.
- 5 Selroos O, Halme M. The effect of a Volumatic spacer and mouth rinsing on systemic absorption of inhaled corticosteroids from a metered dose inhaler and dry powder inhaler. *Thorax* 1991;46:891-4.
- 6 Brown P, Blundell G, Greening A, Crompton G. Do large volume spacer devices reduce systemic effects of high dose inhaled corticosteroids? *Thorax* 1990;45:736-9.
- 7 O'Callaghan C, Barry PW. Spacer devices in the treatment of asthma. *BMJ* 1997;314:1061-2.

## Radiosurgery for brain tumours

Triumph of marketing over evidence based medicine

Recent publicity surrounding the opening of a private radiosurgery facility in the United Kingdom suggested near miraculous properties for a radiation technique developed over 30 years ago. According to media reports, "many potentially fatal brain conditions which are inoperable using conventional surgery can now be treated successfully."<sup>1</sup> This form of marketing is misleading and offers false hope.

Radiosurgery is a term applied to high precision localised irradiation given in one session. One technique uses cobalt sources arranged in a hemisphere and focused on to a central target (described as a gamma knife). A gamma knife unit has been in operation in Sheffield since 1986. Identical high precision radiosurgery can be delivered by appropriately adjusted linear accelerators and has been available in Britain since 1989. Currently, at least six radiosurgery facilities are available to NHS patients. The limited usefulness of the technique for treating brain tumours suggests that the existing NHS facilities are sufficient for the expected workload.

The aim of radiosurgery is to deliver a sphere of high dose irradiation more localised than would be achieved with conventional radiotherapy. However, this is possible only for small lesions less than 3.5-4 cm in diameter. Radiosurgery was used initially for treating inoperable arteriovenous malformations and subsequently for treating acoustic neuromas, solitary brain metastases, and a mixture of other tumours. Despite many years of experience, there is no single randomised trial or robust case-control study testing the efficacy and safety of radiosurgery in comparison with other established treatments. Most reports claiming benefit are from retrospective studies of enthusiastic application of radiosurgery to patients with small brain tumours.

It is generally agreed that single fraction radiosurgery obliterates 80-90% of small arteriovenous malformations. The aim is to reduce the risk of subsequent haemorrhage from an annual untreated rate of rebleeding of 2-4%. In the first two years after radiosurgery the reported annual rebleeding rate is 4-8%,<sup>2,3</sup> and long term data on the incidence of rebleeding at 5-10 years are poor. No information exists on the survival of treated compared with untreated patients. The treatment is not without toxicity: the risk of radiation induced damage seen on magnetic resonance imaging is 20-30% for 2 cm and 40-50% for 3 cm diameter lesions, and these are often symptomatic when in eloquent regions of the brain.<sup>4</sup>

The tumour control of acoustic neuroma after radiosurgery is 91% at five years with a 17% risk of VIIth and a 45% risk of VIIIth neuropathy at five years.<sup>5</sup> Radiosurgery has been advocated for patients with other benign tumours. Early results suggest a recurrence rate of small benign meningiomas of >10% at five years with a 6% risk of neurological toxicity.<sup>6</sup> Long term tumour control of pituitary adenoma after radiosurgery is not known. However,

damage to the optic apparatus, causing visual impairment, has been reported in  $3.4\%^7$  and  $24\%^8$  of patients after radiosurgery at two years, and 30% patients developed temporal lobe damage.9 Optic neuropathy is related to the proximity of the tumour to the optic apparatus and limits the technique to small sellar lesions. In contrast, the risk of radiation induced visual impairment after conventional fractionated radiotherapy is 1-2%, with a tumour control rate of about 90% at 20 years for adenomas of all sizes.<sup>10</sup> Radiosurgery of benign pituitary adenomas and meningiomas is associated with mortality ranging from 1.6%7 to 24%.11 The deaths are a direct consequence of damage from high dose single fraction radiation and have not been reported after fractionated treatment.

Few effective treatments exist for brain metastases and malignant gliomas, and patients will accept any offer of hope. Radiosurgery is a non-invasive alternative to surgery for solitary brain metastases. The median survival is 6-12 months and is related to performance and the state of systemic malignancy.12 Radiosurgery has no advantage over whole brain radiotherapy for patients with multiple brain metastases.13

Radiosurgery alone is not the appropriate primary therapy for malignant gliomas. However, a boost after conventional surgery and radiotherapy of malignant glioma is claimed to be associated with marginal prolongation of survival, but this may be explained by patient selection.<sup>14</sup> Two multicentre randomised studies in the United States and Europe are currently examining this issue. Patients with malignant brain tumours should be encouraged to take part in trials to define the role of radiosurgery in treatment.

Radiosurgery as delivered by the gamma knife has major limitations. Each "shot" consists of a small radiation sphere 4-18 mm in diameter, and these need to be multiple for the treatment of larger lesions. In contrast, linear accelerator techniques offer the possibility of treating larger and moreirregular lesions with a technique described as conformal stereotactic radiotherapy. Single fraction radiation as delivered by the gamma knife in doses greater than 8 Gy to critical structures is associated with a high risk of injury. Giving treatment in multiple small doses (the principle of fractionation) allows for higher radiation doses to the tumour without increased risk of damaging the central nervous system. Conformal stereotactic radiotherapy coupled with fractionation is increasingly being explored as a potentially safer method of delivering high precision localised irradiation.

Activity is often equated with progress. The statement that "about 80 000 people have been treated with the gamma knife world wide"15 reflects uncontrolled spread of an unproved technique and the power of marketing. The limited information available suggests that radiosurgery should be fully evaluated in well designed prospective studies. On present evidence single fraction radiosurgery for brain tumours is associated with higher toxicity than is seen with fractionated irradiation, so far without the reassurance of long term efficacy.

## Michael Brada Senior lecturer in clinical oncology

Institute of Cancer Research and Royal Marsden NHS Trust, Sutton, Surrey SM2 5PT (mbrada@icr.ac.uk)

## Garth Cruickshank Professor of neurosurgery

Queen Elizabeth Hospital, Birmingham B15 2TH

- 1 Hall C. Brain surgery without scalpels or anaesthetic. Daily Telegraph 1998 Sep 8:10.
- 2 Colombo F, Pozza F, Chierego G, Casentini L, De Luca G, Francescon P. Linear accelerator radiosurgery of cerebral arteriovenous malforma-Pollock BE, Flickinger JC, Lunsford LD, Bissonette DJ, Kondziolka D.
- Hemorrhage risk after stereotactic radiosurgery of cerebral arteriovenous malformations. *Neurosurgery* 1996;38:652-61. Flickinger JC, Kondziolka D, Pollock BE, Maitz AH, Lunsford LD.
- 4 Complications from arteriovenous malformation radiosurgery: multivariate analysis and risk modeling. Int J Radiat Oncol Biol Phys 1997; 38:485-90.
- Flickinger JC, Kondziolka D, Pollock BE, Lunsford LD. Evolution in technique for vestibular schwannoma radiosurgery and effect on outcome. Int Radiat Oncol Biol Phys 1996:36:275-80.
- Hakim R, Alexander E III, Loeffler JS, Shrieve DC, Wen P, Fallon MP, et al. Results of linear accelerator-based radiosurgery for intracranial menin-giomas. *Neurosurgery* 1998;42:446-53. Witt CW, Kondziolka D, Flickinger JC, Lunsford LD. Stereotactic
- radiosurgery for pituitary tumours. In: Kondziolka D, ed. Radiosurgery 1995. Basle: Karger, 1996:55-65. Rocher FP, Sentenac I, Berger C, Marquis I, Romestaing P, Gerard JP.
- Stereotactic radiosurgery: the Lyon experience. Acta Neurochir Wien 1995:63:109-14.
- Mitsumori M, Shrieve D, Alexander E, et al. Initial clinical results of LINAC-based stereotactic radiosurgery and stereotactic radiotherapy for pituitary adenomas. Int J Radiat Oncol Biol Phys 1998;42:573-80. 10 McCord MW, Buatti JM, Fennell EM, Mendenhall WM, Marcus RB Jr,
- McCord MW, Buatu JM, Fennen EM, Mendenhai WM, Marcus RB JF, Rhoton AL, et al. Radiotherapy for pituitary adenoma: long-term outcome and sequelae. *Int J Radiat Oncol Biol Phys* 1997;39:437-44.
  Engenhart R, Kimmig BN, Höver KH, Wowra B, Sturm V, van Kaick G, et al. Stereotactic single high dose radiation therapy of benign intracranial
- meningiomas. *Int J Radiat Oncol Biol Phys* 1990;19:1021-6.
  Alexander E III, Moriarty TM, Davis RB, Wen PY, Fine HA, Black PM, et al. Stereotactic radiosurgery for the definitive, noninvasive treatment of brain metastases. J Natl Cancer Inst 1995;87:34-40.
- 13 Joseph J, Adler JR, Cox RS, Hancock SL. Linear accelerator based stereo-taxic radiosurgery for brain metastases: the influence of number of lesions on survival. J Clin Oncol 1996;14:1085-92.
- 14 Curran WJ Jr, Scott CB, Weinstein AS, Martin LA, Nelson JS, Phillips TL, et al. Survival comparison of radiosurgery eligible and ineligible malignant glioma patients treated with hyperfractionated radiation therapy and carmustine: a report of Radiation Therapy Oncology Group 83 02. J Clin Oncol 1993;11:857-62.
- 15 Laurance J. Hospital's virtual knife in a helmet marks the dawn of bloodless surgery. Independent 1998; Sep 8:6.

## Points for pain: waiting list priority scoring systems

May be the way forward, but we need to learn more about their effects

octors have long worried that the British government's emphasis on the number of people on waiting lists, and the time they spend there, obscures the need to treat patients according to clinical urgency. This concern has been voiced most recently in a report from the BMA,<sup>1 2</sup> though others have gone further and pointed to the futility of pursuing policies to reduce, or even abolish, waiting lists.3 4 The BMA

warns that additional funds earmarked for reducing NHS waiting lists and waiting times will provide an incentive for operating on large numbers of minor cases, leaving more urgent cases and potentially cost effective treatments to wait. The danger with such initiatives is that they provide only temporary relief and do not address the underlying problem of ensuring that waiting lists operate as an efficient and

BMI 1999:318:412-4