Authors' objectives
To assess current evidence for gamma knife radiosurgery in the indications of arteriovenous malformations (AVMs), cerebral metastases (CMs) and acoustic neuroma (AN).

Searching
Searches were conducted in the following databases (to March 2000): MEDLINE, PREMEDLINE, HealthSTAR, Current Contents, EMBASE, the Cochrane Library, ISTAHC, DARE, NHS EED and HTA; the search terms were provided. For AVMs and AN, the databases were searched from their commencement. For CMs, they were searched from 1997 onwards, as a prior review of this topic was located.

The American Association of Neurological Surgeons and Congress of Neurological Surgeons Meeting Abstract Archive was also searched, as was the table of contents of Radiosurgery (this journal was not indexed by any of the databases involved in the searches). Additional electronic searches included a variety of internet sites (details provided).

Study selection
Study designs of evaluations included in the review
No a priori criterion relating to study design was established. With the exception of one trial for CMs, all the studies identified were case series and lacked control groups.

Specific interventions included in the review
Studies of cranial radiotherapy were included. Radiotherapy could be delivered by a gamma knife treatment unit, by linear accelerator (LINAC), or by charged-particle therapy units. For some of the questions covered by the review, the comparator of interest was neurosurgery. The intervention and comparator, in parentheses, for each question covered by the review were as follows.

AVMs: stereotactic radiosurgery with gamma knife (stereotactic radiosurgery with LINAC); stereotactic radiosurgery (neurosurgery).

CMs: stereotactic radiosurgery with gamma knife (stereotactic radiosurgery with LINAC); stereotactic radiosurgery plus whole brain radiotherapy, WBRT (WBRT alone); stereotactic radiosurgery plus WBRT (stereotactic radiosurgery alone).

Brachytherapy, interstitial radiotherapy and interstitial radiosurgery were excluded.

AN: stereotactic radiosurgery with gamma knife (stereotactic radiosurgery with LINAC); stereotactic radiosurgery (surgery alone).

Participants included in the review
Studies investigating patients with one of three conditions (i.e. AVMs, CMs, or AN) were eligible. Within each condition, there were separate questions relating to individual groups of patients. The groups of patients were as follows.

AVMs: patients with AVMs in whom intervention is indicated, e.g. those with a previous bleed or ‘expanding’ haematoma, or progressive neurological deficit; patients with cerebral AVMs in whom previous intervention has been unsuccessful in achieving complete obliteration.

Patients with angiographically occult vascular malformations, venous angioma, low- or high-flow carotid cavernous fistulae, and cerebral cavernous malformation were excluded.
CMs: patients with brain metastases (single or multiple lesions) who are suitable for stereotactic radiosurgery.

AN: patients with an AN who have received surgery; patients with an AN who are unsuitable for surgery; patients with an AN; patients with hearing loss, cranial nerve abnormality, local control, other complications (e.g. oedema or haemorrhage).

A priori subgroups were listed for the AVM and CM questions.

Outcomes assessed in the review
AVMs: the primary outcome measures were survival (event free), obliteration of disease (imaging evidence of obliteration on angiogram), intracranial haemorrhage (recurrent) and therapeutic index (response rate divided by the rate of radiation-induced complications). The secondary outcome measures were procedural success (morbidity, complications and mortality rates), quality of life (short and long term), symptoms of disease (e.g. seizure, headache, neurological deficit), safety (short- and long-term side-effects of treatment) and cost.

CMs: the outcome measures were survival, control of lesion and freedom from progression, quality of life (short and long term), symptoms of disease, side-effects of treatment and cost.

AN: the outcomes were hearing, cranial nerve abnormality, local control and other complications (e.g. oedema or haemorrhage).

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

Methods of synthesis
How were the studies combined?
The studies were grouped by the indication for treatment, then further grouped by the method used to administer the treatment.

How were differences between studies investigated?
Differences between the studies were examined narratively.

Results of the review
The review included the following numbers of studies:

for AVMs, 14 case series (n=3,779) of gamma knife surgery, 18 case series (n=1,717) of LINAC radiosurgery and 10 publications, including 12 case series (n=812), of neurological microsurgery;

for CMs, 11 studies (n=668), comprising 1 randomised controlled trial (n=27) and 10 case series (n=641), of gamma knife radiosurgery and 7 case series (n=528) of LINAC radiosurgery;

for AN, 6 case series (n=601) of gamma knife radiosurgery.

AVMs.
Patients treated with microsurgery achieved complete excision rates of 85 to 100%. This increased to 94 to 100% for patients with small, easily accessible lesions. The literature reported that obliteration rates for radiosurgery are likely to be an overestimation of the true rate of AVM obliteration because of inadequate patient follow-up, and the fact that only a proportion of patients eligible for angiography at any given time point actually undergo the procedure. The 2-year obliteration rates (when reported as a percentage of those patients eligible for angiography) ranged from 26 to 45% for gamma knife radiosurgery, and from 44 to 68% for LINAC radiosurgery.

CMs.

The single, small randomised trial suggested that there may be slightly improved local control for patients treated with radiosurgery plus WBRT compared with WBRT alone. There was, however, no survival benefit for these patients. The results of uncontrolled case series generally supported those of the randomised trial.

AN.

Microsurgical excision resulted in complete excision rates of close to 100% (in patients particularly selected for surgery). Radiosurgical treatment resulted in tumour control rates (i.e. stability or regression of tumour) of between 80 and 100%.

**Cost information**

The authors reported that the cost estimates suggest a ratio of gamma knife equipment cost per treatment to LINAC equipment cost per treatment of 1.7 to 2.9, i.e. the gamma knife was 1.7 to 2.9 times more expensive than using a LINAC, depending on the costing scenario examined. The authors stated that, given the lack of information on safety and effectiveness, they could not report on the cost-effectiveness.

**Authors' conclusions**

The poor methodological quality of published data precluded any definitive assessment of the safety and efficacy of gamma knife radiosurgery as a treatment option for AVMs, CMs and AN. Due to differences in the characteristics of the patients treated, it was not possible to determine whether radiosurgery treatment is superior to treatment with conventional methods (e.g. surgery). There was also insufficient information to determine conclusively whether one method of radiosurgery is superior to another.

Microsurgical resection remains an acceptable therapeutic intervention, particularly for patients with small, easily accessible AVMs and AN.

Radiosurgery may be an effective treatment for selected groups of patients with AVMs and AN, e.g. patients with surgically inaccessible lesions or co-morbidities that preclude surgical intervention.

Outcomes for patients with CMs are likely to be influenced more by baseline prognostic factors than by the type of treatment.

The evidence did not indicate a difference in outcomes for patients treated with gamma knife or LINAC radiosurgery.

**CRD commentary**

This review addressed a number of specific questions on three separate diseases. However, in presenting the results of the reviews to answer these questions, all the questions relating to each disease were combined. It is unclear whether the results presented cover all ten of the questions posed.

The review authors provided comprehensive information on the searches they conducted to locate information. While it was not explicitly stated, it appears that they did not apply any language restrictions. However, it also appears that they searched only for published studies.

The participants and outcomes of interest were clearly stated. Some details of the intervention and comparators of
interest were given, whereas some information of importance to these was not considered. As with any form of radiotherapy, the dose and fractionation schedule were not included in the inclusion criteria. It appears that most stereotactic treatments were non-fractionated, but the review authors did not report the doses used in gamma knife, LINAC or WBRT. No information on the fractionation of WBRT was provided.

The authors provided considerable information on the included studies. Given the clinical heterogeneity, the decision not to attempt a meta-analysis was appropriate. The conclusions appear to follow from the information presented.

Implications of the review for practice and research
Practice: 'Since there is currently insufficient evidence on comparative safety, effectiveness and cost-effectiveness pertaining to gamma knife radiosurgery, MSAC recommended that additional public funding should not be supported at this time for this procedure.'

Research: The authors did not define any avenues for future research. It appears that comparisons between radiosurgery and neurosurgery, and between different methods of achieving a therapeutic radiation dose, may be warranted.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.