

STEREOTACTIC RADIOSURGERY/ STEROTACTIC RADIOTHERAPY FOR PILOCYTIC ASTROCYTOMA

QUESTIONS TO BE ADDRESSED:

1. What is the evidence for the clinical effectiveness of stereotactic radiosurgery/ stereotactic radiotherapy for pilocytic astrocytoma compared to other treatment modalities?
2. What is the evidence for the cost-effectiveness of stereotactic radiosurgery/ stereotactic radiotherapy for pilocytic astrocytoma compared to other treatment modalities?

SUMMARY

Background:

- Pilocytic astrocytomas are low-grade glial brain tumours. They are typically well-differentiated, slow-growing and non-invasive and are most commonly found in children and young adults. The incidence of pilocytic astrocytomas is 0.37 per 100,000 persons per year.
- Surgical resection is the preferred first-line treatment for pilocytic astrocytomas where a total or near-total resection can be achieved with acceptable risk. Stereotactic radiosurgery and stereotactic radiotherapy can be used in cases of incomplete surgical resection to treat residual tumour or to treat tumours that have progressed or recurred following surgery.
- Stereotactic radiotherapy (SRT) and stereotactic radiosurgery (SRS) use focused radiation beams to deliver radiation to a specific target with minimal radiation exposure to normal adjacent tissue. In stereotactic radiosurgery the radiation is delivered in a single treatment.

Clinical Effectiveness:

- We did not identify any studies comparing SRS or SRT to other treatments.
- We included seven uncontrolled observational studies (n=177) with ten or more pilocytic astrocytoma patients who had undergone previous surgery¹ with subsequent SRS or SRT. Six studies were retrospective reviews of patients at single institutions and one study reviewed clinical outcomes and activities of daily living for 38 patients recruited prospectively. The median follow-up period ranged from 28 months to 96 months. The study populations were small and heterogeneous in terms of age range, follow-up period and treatments received prior to SRS and SRT.
- There was some variation in the study results. Tumour control (reported by six studies) varied from 50% to 95%. Progression-free survival at one year ranged from 65% to 92% in three studies. Medium-term progression-free survival (at five years or at last follow-up at a median of approximately three years) ranged from 32% to 83% in four studies, and ten-year progression-free survival ranged from 17% to 86% in two studies. Overall survival was generally high; in all of the included studies it was at least 70% at all time-points.
- Better outcomes were associated with non-cystic lesions, smaller tumour volume, newly diagnosed or residual tumour (compared to recurrent tumour), prior surgical intervention comprising total or partial resection compared to biopsy as the prior surgical intervention,

¹ The identified studies categorised previous surgery or initial surgical management as total resection, partial resection or biopsy.

and no brainstem involvement. Worse outcomes were associated with previous radiotherapy, multifocal tumours, older patient age and lower radiosurgical tumour dose.

- One study showed improvement on two measures of activities of daily living from the baseline at four to six weeks after surgery to follow-up at six months, two and three years after SRT.

Cost-Effectiveness:

- We did not identify any studies on the cost-effectiveness of radiosurgery/ stereotactic radiotherapy for pilocytic astrocytoma.

Safety:

- Rates of adverse events attributed to SRS or SRT were generally low. One study reported symptomatic oedema in just under half of their study population.

1 Context

1.1 Introduction

Pilocytic astrocytomas are low-grade glial brain tumours categorised as World Health Organization (WHO) grade 1 astrocytomas [1]. They are typically well-differentiated, slow-growing and non-invasive [2;3] and are most commonly found in children and young adults [1]. They can be cystic or solid tumours or a combination of both [4] and are usually located in either the cerebellum or in proximity to the brainstem [5]. The symptoms of pilocytic astrocytomas can include changes in behaviour, headaches and vomiting, lack of co-ordination and loss of balance, memory loss and seizures [6].

Surgical resection is the preferred first-line treatment for pilocytic astrocytomas where a total or near-total resection can be achieved with acceptable risk [2]. Complete surgical resection is not always possible due to the location of the tumour [3]. The population of interest to this review is patients with pilocytic astrocytoma, residual, recurrent or progressive after previous surgery¹ where further surgery is deemed too high risk [8].

Stereotactic radiosurgery and stereotactic radiotherapy can be used in cases of incomplete surgical resection to treat residual tumour [3] or to treat tumours that have progressed or recurred following surgery [4].

1.2 Existing national policies and guidance

We did not identify any guidance from the National Institute of Health and Care Excellence (NICE) on stereotactic radiosurgery or stereotactic radiotherapy for pilocytic astrocytoma.

2 Epidemiology

The incidence of pilocytic astrocytomas is 0.37 per 100,000 persons per year [6]. This equates to approximately 200 cases per year in England. It is most commonly found in children but can occur in adults [5]. The cystic form of pilocytic astrocytoma is found in more than 75% of patients [4].

3 The intervention

The interventions of interest in this review are stereotactic radiosurgery and stereotactic radiotherapy.

Stereotactic radiotherapy (SRT) and stereotactic radiosurgery (SRS) use focused radiation beams to deliver radiation to a specific target with minimal radiation exposure to normal adjacent tissue [2;3;7]. In stereotactic radiosurgery the radiation is delivered in a single treatment [3]. A fixation device is used to immobilise the head during delivery [7].

The outcomes of interest in this review are: long term tumour control/ cure rate; proportion of patients free from progressive symptoms; proportion of patients with maintenance/ improvement in quality of life; need for repeat or alternative procedures; recovery time after treatment and incidence and nature of adverse events [8].

Outcome measures used to assess activities of daily living in the included studies are described below:

- Modified Barthel's Index (MBI) - assesses functional activities such as eating, dressing, bathing, mobility and bowel/ bladder function on a five point scale that ranges from 'unable to perform task' to 'fully independent'. The maximum total score is 100 [9].
- Karnofsky Performance Status (KPS) – assesses ability to perform ordinary tasks. The maximum score is 100. Higher scores imply better performance.²

4 Findings

A search of Medline, Embase, Cochrane Library, TRIP and NICE Evidence was performed on the 6th November 2015 for studies published in English since 2000. Case reports, conference papers, letters and commentary were excluded. Details of the search strategy are provided in Section 7.

We included seven uncontrolled observational studies with a total of 177 patients. Six studies were retrospective reviews of patients at single institutions and one study was a review of clinical outcomes and activities of daily living for 38 patients recruited prospectively. The median follow-up periods ranged from 28 months to 96 months. Five studies were conducted in the United States, one in Sweden and one in India.

We did not identify any studies comparing SRS or SRT to other treatments. Many of the identified studies included tumours of various histologies. In order to prioritise the best available evidence we have only included studies with separate results for 10 or more pilocytic astrocytoma patients.

There were a number of reasons why studies identified by the literature search did not meet the criteria for inclusion in this review. These included:

- Intervention not SRS or SRT
- Included less than 10 patients with pilocytic astrocytoma
- No separate reporting of results for pilocytic astrocytoma patients receiving SRS or SRT.

² <http://www.cancer.gov/publications/dictionaries/cancer-terms?cdrid=44156>

4.1 Evidence of effectiveness

Of the seven included studies, five considered SRS [1;2;4;5;10], one considered SRT [9] and one considered both SRS and SRT [3].

Tumour control was reported by six of the seven studies and varied from 50% [1] to 95% [5]. The study with the lowest reported tumour control had a study population that only included adults, however all studies had populations with a wide age range. Progression-free survival at one year ranged from 65% to 92% in three studies [1;2;4]. Medium-term progression-free survival (at five years or at last follow-up at a median of approximately three years) ranged from 32% to 83% [1;2;3;4]. Ten-year progression-free survival was 17% in one study [2]. In the other study reporting 10-year progression free survival, this was 86% for newly diagnosed patients who had a biopsy, 57% for patients who had a total resection and recurrence and 46% for patients who had a partial resection and recurrence [4]. One study of patients receiving SRT reported progression-free survival of 82% after a mean follow-up of 22 months [9]. Overall survival was generally high; in all studies it was at least 70% at all time-points.

Four studies investigated factors influencing outcomes. Worse outcomes were associated with previous radiotherapy [2;10], multifocal tumours [10], older patient age [10] and lower radiosurgical tumour dose [10]. Better outcomes were associated with non-cystic lesions [4], smaller tumour volume [4], newly diagnosed or residual tumour (versus recurrence) [4], prior surgical intervention comprising total or partial resection (versus biopsy as the prior surgical intervention) [1] and no brainstem involvement [4].

Six studies (n=150) provided details of further treatment received after SRS or SRT [1;2;3;4;5;10]. The numbers of patients receiving further treatment across all the included studies were:

- Further surgery (n=14)
- Stereotactic cyst evacuation (n=7)
- Chemotherapy (n=6)
- Stereotactic intracavitary irradiation with phosphorus-32 (n=6)
- Repeat SRS (n=4)
- Ventricular peritoneal (VP) shunt (n=4)
- Stereotactic intracavitary irradiation with phosphorus-32 and surgery (n=2)
- Supportive care only (n=2)
- Chemotherapy and radiotherapy (n=1)
- Fractionated radiation therapy (n=1).

Only one study [9] assessed activities of daily living. This showed improvement in two measures of activities of daily living from the baseline, four to six weeks after surgery, to follow-up at six months, two and three years after SRT. Other studies reported on elements of quality of life, for example, one study reported that nine of 11 patients had an improvement in their pre-SRS symptoms after the procedure [2], whereas another study reported that nine of 14 patients reported no change in neurological outcomes and five reported that neurological outcomes were worse [1].

None of the studies reported recovery time after treatment.

The evidence identified is from uncontrolled observation studies which represent lower quality evidence.

Safety issues are discussed in section 4.4.

Table 1: Clinical effectiveness of SRS/ SRT for pilocytic astrocytoma

Study	Population	Intervention	Results	Comments
<p>Hallemeier et al (2012) [2]</p> <p>Retrospective review of patients at one centre treated between 1992 and 2005</p> <p>US</p>	<p>Patients with recurrent or unresectable PA</p> <p>N=18 (20 lesions)</p> <p>Median age 23 years (range 4 to 56)</p> <p>Median follow-up 96 months (range 6 to 180 months)</p>	SRS	<p>Overall survival (from SRS):</p> <ul style="list-style-type: none"> • 1 year: 94% • 5 years: 71% • 10 years: 71% <p>PFS (from SRS):</p> <ul style="list-style-type: none"> • 1 year: 65% • 5 years: 41% • 10 years: 17% <p>Prior external-beam radiotherapy associated with inferior 5-year PFS (71% vs. 20%, p=0.008)</p> <p>Tumour control was achieved for 11 lesions (55%)</p> <p>Treatment for solid tumour progression after SRS after a median of 0.8 years:</p> <ul style="list-style-type: none"> • Systemic chemotherapy (3 patients) • Further surgery (1 patient) • Supportive care only (1 patient) <p>Treatment for distant progression after SRS (2 within 1 year, 1 after 8.3 years):</p> <ul style="list-style-type: none"> • Systemic chemotherapy and radiotherapy (1 patient) • Repeat SRS (1 patient) • Supportive care only (1 patient) <p>Treatment for tumour associated cyst development or progression after SRS after a median of 2.6 years:</p> <ul style="list-style-type: none"> • Intracavitary phosphorus-32 instillation and surgical excision (2 patients) • Intracavitary phosphorus-32 instillation (1 patient) • Surgical excision (1 patient) <p>9/ 11 patients had improvement of their pre-SRS symptoms after the procedure</p>	<p>Of the 18 patients, 7 had prior subtotal resection, 4 had prior gross total resection and 7 had prior biopsy</p> <p>Biopsy was categorised as 'initial surgery' by the authors.</p> <p>Results not provided separately for patients with subtotal resection, gross resection or biopsy</p> <p>10/ 18 patients had received prior external-beam radiotherapy</p> <p>4/18 patients had received prior systemic chemotherapy</p>
Lizarraga et al (2012) [3]	Patients with progressive residual	SRT (n=9)	Disease-specific survival to last follow-up was 91.7%	None of the patients had received adjuvant

<p>Retrospective review of patients at one centre treated between 1995 and 2010</p> <p>US</p>	<p>PA following prior surgery</p> <p>N=12</p> <p>Median age 21 years (range 5 to 41)</p> <p>Median follow-up 37.5 months (range 3 to 168 months)</p>	<p>SRS (n=3)</p>	<p>PFS at last follow up was 73%</p> <p>Tumour control was achieved in 9 patients (75%)</p> <p>3 patients had tumour progression post-treatment (all within one year of treatment) and received:</p> <ul style="list-style-type: none"> • Surgery (2 patients) • A VP shunt (1 patient) 	<p>chemotherapy or radiotherapy before SRS or SRT</p>
<p>Kano et al (2009) [1]</p> <p>Retrospective review of patients at one centre treated between 1994 and 2006</p> <p>US</p>	<p>Patients (adults) with PA with prior surgical management</p> <p>N=14</p> <p>Median age 32 years (range 19 to 52)</p> <p>Median follow-up 36.3 months (range 6 to 109 months)</p>	<p>SRS</p>	<p>Overall survival (from SRS):</p> <ul style="list-style-type: none"> • 1 year: 100% • 3 years: 88.9% • 5 years: 88.9% <p>PFS (from SRS):</p> <ul style="list-style-type: none"> • 1 year: 83.9% • 3 years: 31.5% • 5 years: 31.5% <p>Tumour control was achieved in 7 patients (50%) (including 2 with prior biopsy and 5 with prior resection)</p> <p>7 patients developed some form of tumour progression after SRS (after a median of 18.6 months) and received:</p> <ul style="list-style-type: none"> • Further surgery (5 patients) • Chemotherapy (1 patient) • A VP shunt (1 patient) <p>Neurological outcome: 'Worse' for 5 patients (including 1 with prior biopsy and 4 with prior resection) and 'no change' for 9 patients</p> <p>Sub-group analysis</p> <p>For patients with prior surgical resection (n=10) PFS was:</p> <ul style="list-style-type: none"> • 1 year: 90.0% • 3 years: 38.6% <p>For patients with prior biopsy (n=4) PFS was:</p>	<p>Of the 14 patients, 10 had prior surgical resection (1 total; 9 partial) and 4 had prior stereotactic biopsy</p> <p>Biopsy was categorised as 'initial surgical management' by the authors</p> <p>Results for sub-groups of patients are presented separately where reported</p> <p>6/ 14 patients had received prior fractionated radiation therapy</p>

			<ul style="list-style-type: none"> • 1 year: 50.0% • 3 years: 0% <p>In univariate analysis, patients with prior surgical resection had significantly better PFS (p=0.027) compared to patients with prior biopsy</p>	
<p>Kano et al (2009) [4]</p> <p>Retrospective review of patients at one centre treated between 1987 and 2006</p> <p>US</p>	<p>Patients (children) with PA with prior surgical management</p> <p>N=50</p> <p>Median age 10.5 years (range 4.2 to 17.9)</p> <p>Median follow-up 55.5 months (range 6 to 190 months)</p>	<p>SRS</p>	<p>Overall survival (from SRS):</p> <ul style="list-style-type: none"> • 1 year: 100% • 5 years: 97.4% • 10 years: 97.4% <p>PFS (from SRS):</p> <ul style="list-style-type: none"> • 1 year: 91.7% • 3 years: 82.8% • 5 years: 70.8% <p>Tumour control was achieved in 38 patients (76%)</p> <p>12 patients developed some form of tumour progression after SRS (range 8.9 to 67.5 months) including 1 with prior biopsy and 7 with prior partial resection and 4 with prior total resection. They received:</p> <ul style="list-style-type: none"> • Repeat SRS (2 patients) • Stereotactic cyst evacuation (4 patients) • Stereotactic intracavitary irradiation with phosphorus-32 (3 patients) • Further surgical resection (1 patient) • Surgical removal after intracavitary irradiation (1 patient) <p>Sub-group analysis</p> <p>PFS at 3 years</p> <ul style="list-style-type: none"> • Newly diagnosed with biopsy (n=11): 86% • Newly diagnosed with partial resection (n=5): 100% • Total resection and recurrence (n=16): 87% • Subtotal resection and recurrence (no prior FRT) (n=13): 69% • Subtotal resection and recurrence (with prior FRT) (n=5): 80% <p>PFS at 10 years:</p>	<p>Of the 50 patients, 39 had prior surgical resection (16 total; 23 partial) and 11 had prior biopsy</p> <p>The 11 patients with prior biopsy had deep seated tumours deemed ineligible for total resection</p> <p>16 patients had SRS for residual tumour; 34 had SRS for recurrent tumour</p> <p>2/ 50 patients had received prior fractionated radiation therapy</p> <p>5/ 50 patients had received prior fractionated radiation therapy and chemotherapy</p> <p>Results for sub-groups of patients are presented separately where reported</p>

			<ul style="list-style-type: none"> Newly diagnosed with biopsy: 86% Total resection and recurrence: 57% Subtotal resection and recurrence (no prior FRT): 46% <p>10-year PFS for other sub-groups not available</p> <p>Tumour control</p> <ul style="list-style-type: none"> Newly diagnosed with biopsy (n=11): 91% Newly diagnosed with partial resection (n=5): 100% Total resection and recurrence (n=16): 76% Subtotal resection and recurrence (no prior FRT) (n=13): 67% Subtotal resection and recurrence (with prior FRT) (n=5): 40% <p>In univariate analysis, improved PFS was associated with:</p> <ul style="list-style-type: none"> Non-cystic lesion (p<0.0001) Smaller tumour volume ($\geq 8\text{cc}$ vs. $< 8\text{cc}$) (p=0.001) No brainstem involvement (p=0.009) Newly diagnosed or residual solid tumour vs. recurrence (p=0.049) 	
<p>Jalali et al (2008) [9]</p> <p>Review of ADL outcomes for patients who received surgery and SRT between 2001 and 2008</p> <p>India</p>	<p>Patients with residual or progressive low-grade gliomas recruited prospectively</p> <p>N=38 (27 PA)</p> <p>Median age 12.5 years (range 5-25)</p> <p>Mean follow-up 22.4 months (SD 21.7):</p>	SRT	<p>Overall survival: 85%</p> <p>PFS: 82%</p> <p>ADL assessed at baseline (post-surgery), and 6 months, 2 years and 3 years after SRT</p> <p>Mean MBS (maximum score 100):</p> <ul style="list-style-type: none"> At baseline: 94.5\pm14.8 (n=38) At 6 months: 97.7\pm7.8 (n=27) At 2 years: 98.1\pm5.5 (n=14) At 3 years: 99\pm1.94 (n=12) <p>Mean KPS scores (maximum score 100):</p> <ul style="list-style-type: none"> At baseline: 81.35 (n=38) At 6 months: 85.23 (n=27) At 2 years: 85.50 (n=14) At 3 years: 88.67 (n=12) 	<p>Most patients had PA. The population also included 5 patients with fibrillary astrocytoma, 4 patients with ependymoma, 1 patient with oligodendroglioma and 1 patient with pleomorphic xanthoastrocytoma</p> <p>24/ 38 had prior partial excision. 14/ 38 had gross residual disease or biopsy only</p> <p>Biopsy was included as a prior neurosurgical procedure by the authors</p> <p>No prior radiation therapy or</p>

			Univariate analysis found no significant difference in improvement in MBS score at 2-year follow-up between patients with biopsy and those with partial excision	chemotherapy reported Baseline scores were usually obtained 4-6 weeks after surgery
Hadjipanayis et al (2002) [10] Retrospective review of patients at one centre. Patients treated over a 13 year period (years not stated) US	Patients with recurrent, residual or unresectable PA N=37 Median age 14 years (range 3 to 52) Median follow-up 28 months (range 3 to 92 months)	SRS	7-year actuarial survival rate: 76% Tumour control achieved in 25 patients (68%) 12 patients developed some form of tumour progression after SRS (range 8.9 to 67.5 months) and received: <ul style="list-style-type: none"> • Cyst drainage (5 patients) • Further cytoreductive surgery (4 patients) • Stereotactic cyst evacuation (3 patients) • Stereotactic intracavitary irradiation with phosphorus-32 (4 patients) • Chemotherapy (2 patients) • Repeat radiosurgery (1 patient) • Fractionated radiation therapy (1 patient) • VP shunt (1 patient) All surviving patients had KPS scores ranging from 80 to 100 at last follow-up Sub-group analysis Tumour control <ul style="list-style-type: none"> • Patients with prior biopsy (n=11): 82% • Patients receiving adjuvant SRS (n=17): 76% • Patients with recurrent tumours (n=20): 60% In univariate analysis, factors significantly predicting worse outcomes were: <ul style="list-style-type: none"> • Multifocal tumours (p=0.001) • Previous fractionated radiation therapy (p=0.001) • Older patient age (p=0.021) • Lower radiosurgical tumour dose (p=0.0076) 	Prior to SRS, 24 patients had near total (n=13) or partial (n=11) removal, 5 patients had an open biopsy and 12 had stereotactic biopsy Biopsy was categorised as a 'prior surgical intervention' by the authors Results for sub-groups of patients are presented separately where reported 9/ 37 patients had received prior fractionated radiation therapy 3 /37 patients had received prior stereotactic cyst drainage 2/37 patients had received prior VP shunt placement
Boethius et al (2002) [5] Retrospective	Patients with residual tumour after surgery N=19	SRS	Tumour control was achieved in 18 patients (95%) One patient who had received SRS following open surgery had tumour recurrence after 5.2 years and was re-treated (details not	Prior to SRS 17 patients had open surgery and 2 had biopsy sampling

review of patients at one centre treated between 1978 and 1997 Sweden	Median age 7 years (range 2-60) Median follow-up 84 months (range 4.8 to 24.0 years)		provided). One patient had several shunt procedures for a tumour cyst that remained a problem 6 years after SRS Overall survival and PFS not reported	2/17 patients had received prior conventional radiotherapy 1/17 patients had received prior brachytherapy
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ADL – activities of daily living; cc – cubic centimetres; FRT – fractionated radiation therapy; KPS – Karnofsky Performance Status; MBS – Modified Barthel Score; PA – pilocytic astrocytoma; PFS – progression-free survival; SD: standard deviation; SRS – stereotactic radiosurgery; SRT – stereotactic radiotherapy; VP shunt – ventricular peritoneal shunt

4.2 Trials in progress

We did not identify any trials in progress on SRS/ SRT for pilocytic astrocytoma from clinicaltrials.gov (December 2015).

4.3 Evidence of cost-effectiveness

We did not identify any studies assessing the cost-effectiveness of SRS/ SRT for pilocytic astrocytoma.

4.4 Safety

Table 2 summarises adverse events associated with SRS/ SRT in the seven included studies.

Table 2: Adverse events associated with SRS/ SRT

Study	Safety results
Hallemeier et al (2012) [2]	<ul style="list-style-type: none">8 patients (44%) developed symptomatic oedema
Kano et al (2009) [4]	<ul style="list-style-type: none">5 patients (10%) had adverse radiation effects1 patient (2%) had significant increase in enhancement and peritumoral oedema causing mass effect requiring hospitalisation1 patient (2%) showed peritumoral oedema with central tumour necrosis but did not require medication1 patient (2%) developed imbalance and peritumoral oedema and received corticosteroids
Jalali et al (2008) [8]	<ul style="list-style-type: none">1 patient (3%) SAE (moyamoya disease)
Hadjipanayis et al (2002) [10]	<ul style="list-style-type: none">2 patients (5%) had temporary worsening of the neurological conditions
Boëthius et al (2002) [5]	<ul style="list-style-type: none">5 patients (26%) had adverse radiation effects (2 with clinical symptoms)2 patients (11%) developed tumour cysts
Lizarraga et al (2012) [3]	Reported no complications attributable to radiation therapy
Kano et al (2009) [1]	Reported no adverse radiation effect or any other morbidity after SRS

SAE – serious adverse event; SRS – stereotactic radiosurgery

In two studies [1;3] there were no adverse events associated with SRS. In three other studies [4;8;10] rates of adverse events were generally low. In one study [5] a quarter of the study sample experienced adverse radiation effects and in another study [2] 44% of the population sample developed symptomatic oedema.

4.5 Summary of section 4

The seven included studies were all uncontrolled observational studies which represent lower quality evidence. Five considered SRS, one considered SRT and one considered both SRS and SRT. The study populations were generally small, with the largest sample size being 50 patients, and heterogeneous in terms of age range and treatments received prior to SRS and SRT.

There was some variation in the results achieved, for example, in the reported tumour control rates (ranging from 50% to 95%) and variable progression-free survival rates. Patients received various further treatments after SRS with further surgery the most common procedure. Overall survival was generally high in all studies at all time points. One study showed improvement in two measures of activities of daily living from the baseline at four to six weeks after surgery to follow-up at six months, two and three years after SRT.

In four studies assessing factors affecting outcomes, worse outcomes were associated with previous radiotherapy, multifocal tumours, older patient age and lower radiosurgical tumour dose. Conversely, better outcomes were associated with total or partial surgical resection (compared to biopsy), non-cystic lesions, smaller tumour volume, newly diagnosed or residual tumour (compared to recurrence), and no brainstem involvement.

The study inclusion period covered more than ten years in six of the seven studies. In two studies the inclusion periods started more than 25 years ago (1978 and 1987 respectively). Given these extended time periods it is likely that changes in treatment practices will be a factor in the results.

Pilocytic astrocytoma is a slow-growing tumour. The follow-up period extended to 15 years or more in three studies, but the median (or mean) follow-up period was less than five years in five of the seven studies.

Rates of adverse events attributed to SRS or SRT were generally low, although one study did report symptomatic oedema in just under half of their study population.

We did not identify any studies assessing the cost-effectiveness of SRS or SRT for pilocytic astrocytoma.

5 Discussion and conclusions

The questions posed at the outset of this review are addressed in turn below.

1. What is the evidence for the clinical effectiveness of stereotactic radiosurgery/ stereotactic radiotherapy for pilocytic astrocytoma compared to other treatment modalities?

We did not identify any studies comparing SRS/ SRT for pilocytic astrocytoma to other treatment modalities. Evidence for the clinical effectiveness of SRS and SRT for pilocytic astrocytoma comes from small uncontrolled observational studies which involved heterogeneous populations and showed variable results. All studies reported tumour control in at least 50% of patients although the follow-up period for different patients varied considerably. Analysis of sub-groups of patients found that worse outcomes were associated with previous radiotherapy, multifocal tumours, older patient age and lower radiosurgical tumour dose, whereas better outcomes were associated with non-cystic lesions, smaller tumour volume, newly diagnosed or residual tumour (versus recurrence), prior surgical intervention of total or partial resection (versus prior surgical intervention of biopsy) and no brainstem involvement. Data for the impact of SRS and SRT for pilocytic astrocytoma on quality of life were limited but improvements in measures of activities of daily living were observed in one study. Rates of adverse events attributed to SRS or SRT were generally low.

Because this evidence is from uncontrolled observational studies it is not possible to draw any strong conclusions about the effectiveness of SRS or SRT in patients with pilocytic astrocytoma who have had prior surgery.

2. What is the evidence for the cost-effectiveness of stereotactic radiosurgery/ stereotactic radiotherapy for pilocytic astrocytoma compared to other treatment modalities?

We did not identify any studies assessing the cost-effectiveness of SRS or SRT for pilocytic astrocytoma.

Competing Interest

All SPH authors have completed the ICMJE uniform disclosure form (www.icmje.org/coi_disclosure.pdf) and declare: grants from NHS England to SPH to undertake the submitted work, no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work

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7 Search Strategy

Table 3: Population, Intervention, Comparator and Outcomes (PICO)

Patients/ population	Patients with pilocytic astrocytoma, residual, recurrent or progressive after previous surgery where further surgery deemed too high risk
Intervention	Stereotactic radiosurgery / stereotactic radiotherapy
Comparison	Surgery Fractionated radiotherapy Proton beam therapy
Outcomes	Clinical effectiveness <ul style="list-style-type: none"> • Long-term tumour control / cure rate • Proportion of patients free from progressive symptoms • Proportion of patients with maintenance/ improvement of quality of life • Incidence and nature of adverse events • Need for repeat or alternative procedures • Recovery time after treatment Cost-effectiveness / cost of treatment

Search date: 6th November 2015

Databases searched: Medline, Embase, Cochrane, TRIP and NICE Evidence Search

Limited to studies published in English from 2000 onwards.

Case reports, conference papers, letters and commentary excluded.

This was a combined search for papers on ependymoma, haemangioblastoma, pilocytic astrocytoma and trigeminal schwannoma, each of which is the subject of a separate evidence review. Only the results for pilocytic astrocytoma are considered in this review.

Embase search strategy

- 1 ependymoma/
- 2 (ependymoma? or ependymal glioma? or subependymal glioma?).ti,ab.
- 3 1 or 2
- 4 hemangioblastoma/
- 5 (h?emangioblastoma? or angioblastoma?).ti,ab.
- 6 4 or 5
- 7 pilocytic astrocytoma/
- 8 (pilocytic astrocytoma? or cystic cerebellar cytoma? or pilomyxoid astrocytoma?).ti,ab.
- 9 7 or 8
- 10 neurilemoma/ and (trigeminal nerve/ or trigeminal nerve disease/)
- 11 (trigeminal adj2 (schwannoma? or neuroilemoma?)).ti,ab.
- 12 10 or 11
- 13 3 or 6 or 9 or 12
- 14 exp stereotactic procedure/
- 15 (stereotactic* or stereotaxic* or sbrr or srr or srs or radiosurg* or radio-surg*).ti,ab.
- 16 (gammaknife or gamma knife or linac or cyberknife or cyber knife).ti,ab.
- 17 14 or 15 or 16
- 18 13 and 17
- 19 case report/
- 20 conference*.pt.
- 21 19 or 20
- 22 18 not 21
- 23 limit 22 to (english language and yr="2000 -Current")