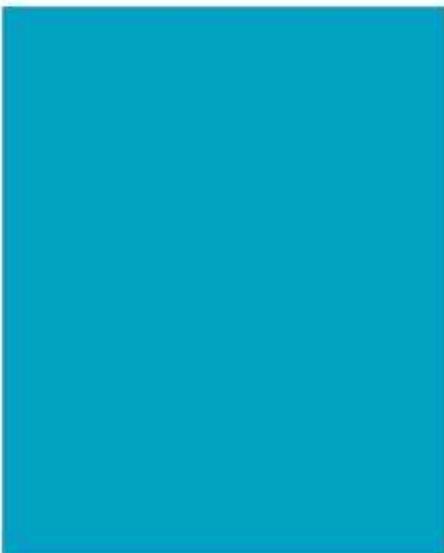


**Clinical Commissioning Policy:  
Stereotactic  
Radiosurgery/Radiotherapy for  
Meningioma**

**September 2013**

**Reference: NHS ENGLAND D05/P/e**



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# NHS England

## **Clinical Commissioning Policy: Stereotactic Radiosurgery / Radiotherapy for Meningioma**

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Radiosurgery**

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## **Policy Statement**

NHS England will commission in accordance with the criteria outlined in this document.

In creating this policy NHS England has reviewed this clinical condition and the options for its treatment. It has considered the place of this treatment in current clinical practice, whether scientific research has shown the treatment to be of benefit to patients, (including how any benefit is balanced against possible risks) and whether its use represents the best use of NHS resources.

This policy document outlines the arrangements for funding of this treatment for the population in England.

## **Equality Statement**

Throughout the production of this document, due regard has been given to eliminate discrimination, harassment and victimisation, to advance equality of opportunity, and to foster good relations between people who share a relevant protected characteristic (as cited in under the Equality Act 2010) and those who do not share it.

## **Plain Language Summary**

A meningioma is a tumour of the meninges, which are the protective membranes around the brain and spinal cord. They can start in any part of the brain or spinal cord, but the most common sites are the cerebral hemispheres of the brain.

Stereotactic radiosurgery (SRS) or stereotactic radiotherapy (SRT) destroys abnormal tissues in the brain by the administration of a strong and highly focused dose of radiation. Microsurgery is the preferred treatment option in the management of patients with meningiomas where the operative risks are low or minimal. This enables histological diagnosis to be confirmed, provides an opportunity for complete excision and permits cytoreduction, even if the tumour origin is not amenable to resection.

However, for tumours located in the skull base, the risks of microsurgery are often substantial, particularly. Evidence has accrued over the past twenty years supporting the use of SRS as a primary treatment for meningiomas that are in anatomically unfavourable locations where microsurgery is deemed to have an unacceptably high risk of neurological deficit. These locations include, but are not confined to, the skull base, the posterior fossa, parasagittal, parafalcine and intraventricular sites.

It is appropriate for clinicians to consider SRS for a small subset of patients with meningioma that are in a difficult and unacceptable high risk anatomical situation where there is evidence of effectiveness for SRS, and where conventional surgery is contra-indicated or the risk of functional disability would be increased through surgery.

## 1. Introduction

This policy considers the use of Stereotactic Radiosurgery (SRS) for patients with meningiomas and states the criteria identifying which patients should be considered for this treatment.

The basic principle of stereotactic radiosurgery (SRS) for this application is the administration of high dose, precisely focused radiation. This enables radiation to be limited to the target area and thus helps minimise collateral damage to surrounding structures as much as possible. Evidence from large numbers of patients indicates that long-term tumour control is achieved in a high proportion of cases.

## 2. Definitions

### **Meningiomas**

Meningiomas are the commonest benign primary brain tumour. Typically they have dural attachments, though rarely can grow in an intraventricular location. They commonly arise over the convexity of the brain, within the parasagittal or parafalcine regions or in any skull base location. Meningiomas may present with focal neurological deficits, seizures, raised intracranial pressure or as an incidental finding. The treatment options are governed by many factors including patient factors (age, performance status, co-morbidity, informed patient choice), tumour-related factors (volume, location, evidence of growth, evidence of calcification) and treatment factors (probability of satisfactory excision, probability of SRS-induced disease control, operative risks, risk of adverse radiation reactions). The absence of symptoms, a heavily calcified tumour or a very small tumour may appropriately lead to conservative management with a radiological surveillance program. This is particularly appropriate in patients with more advanced age in whom symptomatic tumour progression is unlikely to occur. However, in many locations, further growth of the tumour after initial diagnostic imaging, will make treatment of the tumour more difficult, leading to universal agreement that intervention should be considered appropriate.

Meningiomas account for around 18% of adult primary brain tumours. In adults (age 24-84 years) they occur in 2.4 per 100,000 person, years.<sup>1</sup> They are much less frequent in children but occur with increasing frequency in patients over 80 years of age. Typically they have dural attachments, though rarely can grow in an intraventricular location. They commonly arise over the convexity of the brain, within the parasagittal or parafalcine regions or in any skull base location. Meningiomas may present with focal neurological deficits, seizures, symptoms of raised intracranial pressure or as an incidental finding. The CT and MRI appearances are usually sufficiently characteristic to enable a radiological diagnosis to be made with a high degree of certainty. For those meningiomas with a histological diagnosis over 90% are classified as benign (WHO grade 1); 7% of cases are atypical (WHO grade 2) and 2% anaplastic (WHO grade 3).<sup>2</sup>

### **Stereotactic Radiosurgery (SRS) and Stereotactic Radiotherapy (SRT)**

The basic principle of stereotactic radiosurgery (SRS) and stereotactic radiotherapy

(SRT) is the destruction of abnormal tissues, by administration of high dose, precisely focused radiation limiting collateral damage to surrounding tissues as much as possible.

For the purpose of this policy the term “SRS” is used to mean treatment given as a single dose, and “SRT” as a hypofractionated treatment of not more than 5 fractions. This policy applies to both of these approaches. Commissioning arrangements for fractionated treatments utilising a larger number of fractions are beyond the remit of this policy but fall within the Radiotherapy CRG policy remit.

SRS/SRT is a highly conformal radiotherapy treatment to a precisely delineated target volume, delivered using stereotactic localisation techniques. A multidisciplinary team of neurosurgeons or neuro-oncologists, and neuro-radiologists should be involved in SRS case selection, treatment planning and delivery.

### **3. Aim and objectives**

The objectives were to establish:

- If there is sufficiently robust evidence of clinical and cost effectiveness and safety to support the use of SRS for patients with intracranial meningiomas?
- If the evidence is sufficiently robust, what criteria should be used to identify suitable patients to be considered for SRS treatment?

### **4. Epidemiology and needs assessment**

Overall 1.5-1.9% of all cancers registered in England are tumours of the CNS. Data from the eight population-based regional registries in England indicates that the incidence of meningioma in adults aged 25-84 is 2.4/100,000 person-years.<sup>1</sup> The incidence in children and young adults is substantially less than this. The average annual number of cases in adults (aged 25-84) is 996.<sup>1</sup> The median age of presentation is 63 years.<sup>1</sup> Quality data on the relative frequencies of conservative vs. surgery vs. radiation treatment are not well established. The majority of patients for whom treatment is recommended undergo surgical excision with long-term surveillance of the operative site to detect any recurrence or re-growth of residual tumour. The largest published study on meningioma treatment with SRS comprised 4517 patients with 5062 meningiomas accrued from 15 centres over a 16 year period.<sup>3</sup> This represents a crude rate of 19 per centre per annum. 3 of these centres were in the UK (Sheffield, Cromwell Hospital, London Gamma Knife Centre). In the South West of England approximately 7 cases per million have been treated with single fraction SRS annually over the past 7 years (Personal communication, Peter C Whitfield). This equates to an annual rate of treatment of 350 per 50 million per annum.

## 5. Evidence base

Blinded trials cannot be conducted comparing the treatment of meningiomas with SRS and/or microsurgery and/or a conservative approach. Given the fact that many meningiomas occur in critical areas of the brain, outcomes of treatment are potentially compromised by adopting a watch, wait and re-scan policy. The slow growth rate of meningiomas makes the analysis of long-term follow-up mandatory to assess the treatment effect.

The treatment options are governed by many factors including *patient factors* (age, performance status, co-morbidity, informed patient choice), *tumour-related factors* (volume, location, evidence of growth, evidence of calcification) and *treatment factors* (probability of satisfactory excision, probability of achieving disease control with different treatment modalities, operative risks, risk of adverse radiation reactions). The absence of symptoms, a heavily calcified tumour or a very small tumour may appropriately lead to conservative management with a radiological surveillance program. This is particularly appropriate in patients with more advanced age in whom symptomatic tumour progression is unlikely to occur. However, in many locations (e.g. skull base, parasagittal) any degree of tumour enlargement can lead to compression of adjacent neurological structures with associated permanent neurological deficits. Whilst there is universal agreement that intervention is appropriate for many patients with critically placed meningiomas, experienced neurosurgeons must be involved in determining the operative risks and the likelihood of involvement of adjacent structures.

### Natural History

Data on the natural history of untreated meningiomas is limited. Conservative management has been reported in several small, historical studies. Radiological progression is commonly observed (24-76% of cases) and the development of new or progressive neurological symptoms and signs (27.5% to 70%) also occurs over a period of several years.<sup>4-7</sup> In a large (273 meningiomas) recent study, with volumetric tumour measurements, tumour growth was observed in 74% of cases.<sup>8</sup> The growth rates of tumours are variable. Some exhibit linear growth, some exponential growth and some seem to stop growing.<sup>9</sup> The studies are characterised by an inability to reliably predict which tumours will grow and how quickly. Clinical progression is more common in patients with tumours that grow more quickly.<sup>10</sup> Factors that appear to confer very slow progress are patient age over 70 years and heavy calcification of the tumour.<sup>11-15</sup>

### Evidence of Tumour Control

There are many case series published in the literature evaluating the outcome of SRS treatments in patients with meningiomas. The majority of these have focused on the treatment of skull base meningiomas although treatment effects have been established in large numbers of tumours located at other intracranial anatomical locations.<sup>3,16,17</sup> As shown in the table below progression-free survival rates exceed 90% at 5 years in the majority of studies published in the last decade with over 100 recruited patients. Most studies used a marginal dose of 12-15Gy. Morbidity was generally around 5-10%. This is substantially better than the complication rates for complex skull base meningiomas treated with microsurgery.<sup>18</sup> Kondziolka et al

demonstrated that, as with microsurgery and radiation therapy, SRS was less effective at achieving tumour control in Grade 2 and Grade 3 meningiomas: control rates of 50% (at 2 y) and 17% (at 15m) respectively.<sup>16</sup> Other factors reducing the efficacy of SRS include marginal dose of less than 12Gy and large tumour volume.<sup>19</sup>

| <b>Author</b>                    | <b>Number of cases and duration of follow-up</b>                      | <b>Median dose</b> | <b>Outcome</b>                                | <b>Toxicity</b>                   |
|----------------------------------|---|--------------------|---|-----------------------------------|
| Santacrose <sup>3</sup><br>2011  | 4565 cases<br>>26% in non-skull base locations.<br>FU > 60m all cases | 14.0 Gy (+/- 3Gy)  | Control rates<br>95.2% (5y); 88.5% (10y)      | 6.3% temporary;<br>6.6% permanent |
| Pollock <sup>17</sup><br>2012    | 416 cases –<br>81% skull base/<br>tentorial.<br>Median FU<br>60m      | 16.0 Gy            | Local Control<br>rates 96% (5y);<br>89% (10y) | 5% at 1 y<br>11% at 5y            |
| Starke <sup>20</sup><br>2012     | 255 cases<br>Skull base<br>Median FU<br>75m                           | 14Gy               | Local control 96%<br>5y; 79% 10y              | 10%                               |
| Takanashi <sup>21</sup><br>2009  | 101 cases.<br>Skull base.<br>Median FU<br>77m                         | 13.2Gy             | 90% at 5y                                     | 0%                                |
| Iwai <sup>22</sup> 2008          | 108 cases<br>Skull base<br>Median FU<br>86m                           | 12Gy               | 93% at 5y; 83%at<br>10y                       | 6%                                |
| Kondziolka <sup>16</sup><br>2008 | 972 cases.<br>All locations<br>Median FU<br>48m                       | 14Gy               | 87% at 10 and<br>15y                          | 7.7%                              |
| Feigl <sup>23</sup> 2007         | 214 cases<br>Skull base<br>Median FU<br>24m                           | 13.6Gy             | 86.3% at 4y                                   | 6.7%                              |
| Hasegawa <sup>24</sup><br>2007   | 115 cases<br>Skull base<br>Median FU<br>62m                           | 13Gy               | 87% at 5y; 73% at<br>10y                      | 12%                               |
| Kollova <sup>25</sup><br>2007    | 368 cases<br>Skull base<br>Median FU<br>60m                           | 12.5Gy             | 98% at 5y                                     | 15.9%                             |

|                                  |   |        |                           |      |
|----------------------------------|---|--------|---------------------------|------|
| Kreil <sup>26</sup> 2005         | 200 cases<br>Skull base<br>Median FU<br>95m | 12Gy   | 98.5 at 5y; 97% at<br>10y | 4.5% |
| DiBiase <sup>27</sup><br>2004    | 162 cases<br>Skull base<br>Median FU<br>54m | 14Gy   | 86.2% at 5y               | 8.3% |
| Eustacchio <sup>28</sup><br>2002 | 121 cases<br>Skull base<br>Median<br>FU82m  | 13Gy   | 97.8%                     | 6.7% |
| Lee <sup>29</sup> 2002           | 155 cases<br>Skull base<br>Median FU<br>35m | 15Gy   | 93% at 5 and 10y          | 6.7% |
| Nicolato <sup>30</sup><br>2002   | 111 cases<br>Skull base<br>Median FU<br>48m | 14.8Gy | 96% at 5y                 | 8%   |

Volumetric assessment of tumour size (at 6 months and then annually) provides a relevant assessment of response to SRS treatment. In the European Study 58% of tumours reduced in size and 34.5% remained unchanged at a median follow up of 63 months.<sup>3</sup> From a costing perspective, post-operative patients also undergo regular surveillance scans at similar time-points.

SRS provides an effective treatment for meningiomas. When compared to microsurgery it provides:

- shorter hospitalisation
- a less detrimental impact on quality of life
- avoidance of procedural mortality and lower incidence of treatment-related complications

At present the majority of large series describe patients undergoing Gamma Knife treatment. Evidence from LINAC and CyberKnife does appear to provide similar levels of clinical effectiveness. Long-term outcomes need to be audited and reviewed to provide evidence for this. No evidence was identified on which to base comparisons of the relative safety of Gamma Knife, LINAC and CyberKnife.

### **Cost-effectiveness**

There is a lack of evidence addressing the cost-effectiveness of SRS compared to other treatment options for meningiomas in a UK setting. However, there is some evidence from a comparative study between microsurgical costs and radiosurgery costs that, in 1999, the overall costs for microsurgery were more than double the costs of SRS.<sup>31</sup> For patients undergoing SRS rather than microsurgery the cost-

savings to the NHS are likely to be substantial. SRS is usually delivered as a day-case treatment under local anaesthetic. Microsurgical resection is performed under general anaesthetic. Operative times usually extend from 2 to 10 hours or more, according to complexity. Microsurgery patients are managed for 12-24 hours minimum in an intensive care/ high dependency care environment. Hospital stay is usually in the range of 4-10 days but may extend to several months if post-operative deficits and complications (such as CSF leak) occur. This can provide a significant strain upon neurological-rehabilitation resources. In addition, SRS controls disease progression in most patients with low re-treatment rates.

## 6. Rationale behind the policy statement

- The evidence base regarding the effectiveness, cost effectiveness and safety of SRS/SRT for treating meningioma has been used as a basis for this commissioning policy.
- SRS/SRT can be used to treat meningiomas where patient factors (co-morbidity, informed patient choice) and tumour factors (e.g. critical anatomical location) preclude safe microsurgical removal.
- Ongoing monitoring of numbers and outcomes must be undertaken.

## 7. Criteria for commissioning

Indications for stereotactic radiosurgery/radiotherapy include newly diagnosed meningiomas, residual meningioma after microsurgical resection and recurrent meningiomas.

### **Evidence supports the following statements:**

- There is a well established role for SRS in the treatment of patients with intracranial meningiomas
- Any role for fractionated / hypofractionated treatment (SRT) in the management of meningiomas is unproven.
- There is a role for the use of fractionated SRT (more than 5 fractions) in patients with very large skull base meningiomas.

### **Patients meeting all the following criteria will be routinely funded for SRS/SRT:**

- All patients must have undergone prior assessment by the regional neuro-oncology multi-disciplinary team (MDT). The selection of patients for SRS/SRT must include the consideration of surgical or conservative treatment.
- In centres where SRS/SRT is delivered, referral may be made directly to the SRS MDT provided consideration of surgical or conservative options is undertaken. In centres where there is no local SRS service, referral should be initially to the regional neuro-oncology MDT, who can decide on the appropriateness of onward referral to an agreed SRS centre.
- It is appropriate for clinicians to consider SRS for a small subset of patients

with meningioma that are in a difficult and unacceptable high risk anatomical situation where there is evidence of effectiveness for SRS, and where conventional surgery is contra-indicated or the risk of functional disability would be increased through surgery.

All patients being considered for SRS /SRT must be discussed by the specialist MDT at the stereotactic treatment centre and must have specialist neurosurgery input. SRS/SRT must not be recommended without the collective agreement of the MDT.

## **8. Patient pathway**

The service specification for SRS/SRT describes the detail of the care pathways and the key aspects of SRS/SRT services being commissioned and should be referred to in conjunction with this policy.

The service will accept referrals from consultant medical staff and appropriate specialist neuro-oncology MDTs in line with eligibility and referral guidelines. The provider of SRS treatment will discuss all referrals in an SRS MDT prior to accepting the patient for treatment.

The three management options for patients with meningioma are;

- Surgical removal
- Radiation treatment: SRS (single fraction), SRT (2-5 fractions), Multi-fraction treatment (>5 fractions) with or without stereotactic localisation techniques
- No intervention / radiological surveillance

All treatment options must be considered in an MDT for all patients with intracranial meningiomas. These must be discussed with the patient; patient choice is of fundamental importance.

## **9. Governance arrangements**

The service specification for SRS/SRT describes the care pathways and key aspects of SRS/SRT services being commissioned and should be referred to in conjunction with this policy.

## **10. Mechanism for funding**

From July 2013 NHS England became responsible for commissioning Stereotactic Radiosurgery in line with this policy on behalf of the resident population of England.

Funding will be transacted as per local contract agreements and terms.

## **11. Audit requirements**

Clinical governance guidelines state that all British neurosurgical centres are

required to audit their results

Audit requirements will require the following data requirements for each patient:

1. Treatment parameters (including marginal dose)
2. Post-radiosurgery complications (including symptomatic oedema, neurological deficits)
3. Post treatment volumetric assessment of tumour (Suggested at 6 months, annually for 5 years then every 2 years)

*Changes, including addition and/or removal of audit criteria will be negotiated as required to reflect up-to-date practice.*

## **12. Documents which have informed this policy**

2012/13 NHS Standard Contract: Service Specification Contract NSSD 8 Neurosciences (adult (subsection 4.1 Neurosurgery) Stereotactic Radiosurgery and stereotactic radiotherapy.

Please also see reference list below.

## **13. Links to other policies**

This policy follows the principles set out in the ethical framework that govern the commissioning of NHS healthcare and those policies dealing with the approach to experimental treatments and processes for the management of individual funding requests (IFR).

## **14. Date of review**

This policy will be reviewed in April 2016 unless data received indicates that the proposed review date should be brought forward or delayed.

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