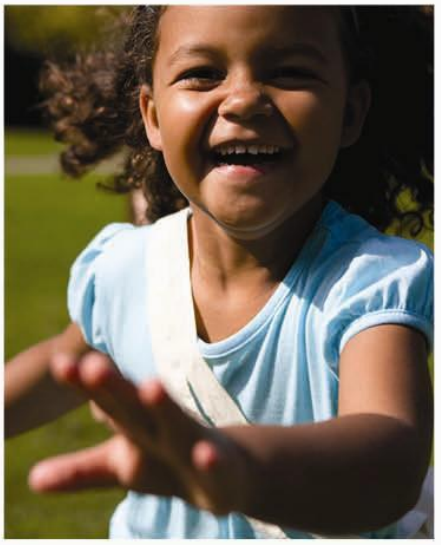
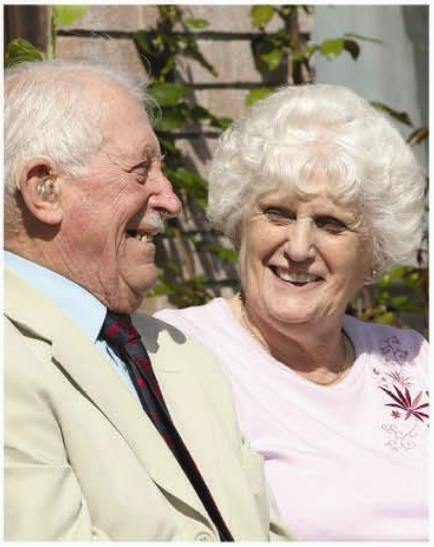
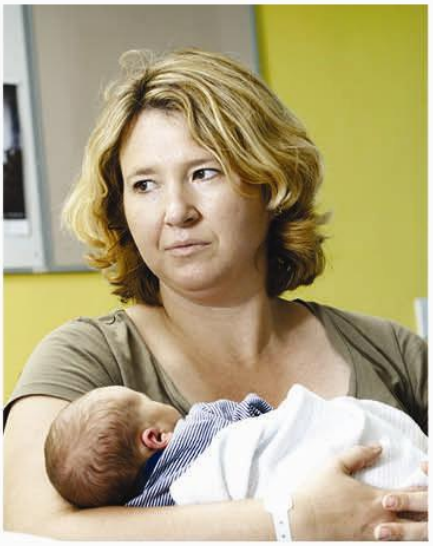
NHS Commissioning Board

Clinical Commissioning Policy: Stereotactic Radiosurgery for Cerebral Arteriovenous Malformations







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NHS Commissioning Board

Clinical Commissioning Policy: Stereotactic Radiosurgery for Cerebral Arteriovenous Malformations

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Prepared by the NHS Commissioning Board Clinical Reference Group for

Stereotactic Radiosurgery

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Contents

Policy Statement

The NHS Commissioning Board (NHS CB) will commission stereotactic radiosurgery (SRS) or stereotactic radiotherapy (SRT) for Cerebral Arteriovenous Malformations (AVMs)
in accordance with the criteria outlined in this document.

In creating this policy the NHS CB 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

The NHS Commissioning Board (NHS CB) has a duty to have regard to the need to reduce health inequalities in access to health services and health outcomes achieved as enshrined in the Health and Social Care Act 2012. The NHS CB is committed to ensuring equality of access and non-discrimination, irrespective of age, disability(including learning disability), gender reassignment, marriage and civil partnership, pregnancy and maternity, race, religion or belief, sex (gender) or sexual orientation. In carrying out its functions, the NHS CB will have due regard to the different needs of different protected equality groups in line with the Equality Act 2010.This document is compliant with the NHS Constitution and the Human Rights Act 1998. This applies to all the activities for which they are responsible, including policy development, review and implementation.

Plain Language Summary

Arteriovenous malformations (AVMs) are networks of coiled feeding arteries and draining veins that are not properly connected by capillaries. They are generally thought to be present from birth and most commonly occur in the brain. High pressure blood flows directly from arteries into veins giving risk of haemorrhage. Cerebral AVMs may present with symptoms such as seizures, neurological deficits and intractable headache. They may be asymptomatic and picked up during the course of investigations for other conditions.

Treatment options include: embolisation (a technique used to block the blood supply to the AVM), microsurgery or radiosurgery (SRS/SRT). For patients meeting the commissioning criteria where an appropriate assessment of long term risk of haemorrhage has been undertaken, treatment with SRS/SRT will be funded. In emergency situations microsurgery is the primary intervention. For all other cerebral AVMs all three modalities (microsurgery, embolization and SRS/SRT) must be considered by clinicians in a multidisciplinary setting.

Information on the outcome of treatments for these patients will be collected and considered when this policy is reviewed.

1. Introduction

The basic principle of stereotactic radiosurgery (SRS) and stereotactic radiotherapy (SRT) is the elimination of a functional disorder, or destruction of abnormal tissues, by administration of a strong and highly focused dose of radiation. The procedure allows radiation to be limited to the target area and thus helps spare the surrounding tissues as much as possible.

This policy considers the use of SRS/SRT to be the standard therapy for patients with cerebral arteriovenous malformations (AVM) and states the criteria to identify which patients should be considered for SRS/SRT.

2. Definitions

Arteriovenous malformations

Cerebral AVMs are networks of coiled feeding arteries and draining veins that are not properly connected by capillaries. They are generally thought to be present from birth and most commonly occur in the brain. AVM lesions are graded using the Spetzler-Martin Grading Scale[1] which is based on the diameter of the lesion, its location and type of venous drainage (Appendix 1). A more recent version of the grading scale has been proposed that reduces the five grades of AVM in to three classes (Appendix 1).[2]

High pressure blood flows directly from arteries into veins giving risk of haemorrhage and subsequent related morbidity and, in some cases, mortality.

Cerebral AVMs may present with symptoms such as intracranial haemorrhage, seizures, neurological deficits and intractable headache or they may be asymptomatic and picked up during the course of investigations for other conditions.[3,4] Approximately 50% of patients present with haemorrhage at initial diagnosis,[3] therefore surgical or radiological treatments are conducted post-haemorrhage in approximately half of patients.

Stereotactic Radiosurgery (SRS) and Stereotactic Radiotherapy (SRT)

The basic principle of stereotactic radiosurgery (SRS) and stereotactic radiotherapy (SRT) is the elimination of a functional disorder, or destruction of abnormal tissues, by administration of a strong and highly focused dose of radiation. The procedure allows radiation to be limited to the target area and thus helps spare the 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.

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

3. Aim and Objectives

The aims of this policy are:

- To identify whether there is sufficiently robust evidence of clinical and cost effectiveness and safety to support the use of SRS/SRT for patients with cerebral AVM
- If the evidence is sufficiently robust, to identify the criteria which should be used to identify suitable patients to be considered for SRS/SRT treatment

4. Criteria for commissioning

A number of procedure selection tools exist for arteriovenous malformations (AVM). No one system is ideal, however for the purpose of this policy the Spetzler Martin (SM) (Appendix 1) is utilised to provide a mechanism of guiding patient selection for stereotactic radiosurgery (SRS) or stereotactic radiotherapy (SRT). In emergency situations microsurgery is the primary intervention. For all other AVMs all three modalities, microsurgery, embolization and SRS/SRT must be considered in a multidisciplinary setting.

Embolisation may be used in isolation or to reduce the size of large lesions and make previously unsuitable AVMs potential candidates for microsurgery or radiosurgery. For patients meeting the commissioning criteria where an appropriate assessment of long term risk of haemorrhage has been undertaken, treatment with SRS/SRT will be funded. Individuals not meeting the criteria will not be routinely funded.

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

Funding will only be released when ALL of the following criteria are met:

- All patients referred for SRS/SRT should have been first assessed through a neuroscience unit based neurovascular multidisciplinary team (MDT).
- The relative benefits and risks of SRS/SRT and microsurgery must be discussed

and recorded in the case notes of all patients for whom SRS/SRT is considered.

- All patients with a non-resectable AVM should be discussed with the relevant SRS/SRT MDT before other treatment such as embolisation are utilised as this may affect efficacy of future SRS/SRT treatments.

The decision to use single dose SRS as compared to hypofractionated SRT should take the following expert opinion in to account. Expert opinion suggests that:

- Stereotactic radiosurgery may be most appropriate for AVMs <4cm maximal diameter AND compact nidus (as opposed to a diffuse malformation or sheet like dural AVM).
- Stereotactic radiotherapy may be most appropriate for AVMs >4cm diameter or volume of >10cm^3 OR where the radiation dose to eloquent brain tissue is above levels of tolerance.

5. Patient pathway

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

Referrals in to the service are accepted from consultant medical staff and appropriate medical MDTs in line with eligibility and referral guidelines. The provider of SRS/SRT treatment will discuss all referrals in an SRS/SRT MDT prior to accepting the patient for treatment.

Prior to commencing treatment, all management risks must be considered, including those associated with diagnosis, surgery, radiotherapy and interventional radiology. These risks include both early and late complications and any remaining risk of further haemorrhage.[2]

Microsurgical removal is the traditional definitive treatment, however endovascular neurosurgery (embolisation) and SRS are also established standard treatments for AVMs[2]. In some cases conservative observation is the most appropriate approach. There is not a definitive step-wise approach to the treatment options for AVM. Recommendations for management are made on a case-by-case basis. However, applying the SM grading scale, lower grade AVMs (grade I and II) may be considered for surgical intervention, medium grade AVMs (grade III) may be treated by a variety of methods and large grade AVMs may be best observed with no treatment or treated with SRT or staged SRS.

6. 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.

7. Epidemiology and needs assessment

Estimations of the incidence and prevalence of AVMs vary widely. On the basis of autopsy findings, the prevalence of AVMs has been estimated to be between 0.06 and 0.11% and the incidence between 1 and 10 per 100,000 people per year.[3] In another study the annual incidence of symptomatic AVMs was 1.2 per 100 000 population.[5] This included those diagnosed after haemorrhage, epilepsy, vascular steal, headaches etc. There was an estimated additional 5% of truly incidental AVM diagnosis (0.06 per 100 000) diagnosed when investigated after head injury or other cerebral pathologies.

Applying the higher figures to the England population of 53million[5] the number of people estimated to have an AVM is between 31,800 and 58,300. The number of new cases expected in a year is approximately 2,650 but may be as low as 32.

It is estimated that 85% of AVMs are diagnosed and graded as SM I – III (23% were grade I, 36% grade II, 25% grade III, 11% grade IV and 5% grade V).[4] The majority of these will be treated by microsurgical resection. Non-surgical patients care may be conservative observation or embolisation, depending on the characteristics of the patient and the AVM.

8. Evidence Base

Evidence can be graded according to the robustness of the study design, giving an indication of the degree to which the evidence should be relied upon when making clinical decisions. The grades of evidence range from level 1 (the most robust) to level 4 (the least robust). The diagram in Appendix 2 outlines the levels of evidence.

An evidence review on the use of SRS/SRT for AVMs was commissioned from the Birmingham University Health Technology Assessment Collaboration in 2010.[1]

No relevant randomised controlled trials (level 1) were found. The review was based on three systematic reviews of case series (level 4)[8,9,10] the most recent of these is from 2002. Case series literature from 2009 report similar results to those reported in the older SRS/SRT case series studies used in the systematic reviews.

No studies were identified that made direct comparisons of the safety, effectiveness

and cost-effectiveness between SRS/RST and microsurgery. There are limitations with making indirect comparisons which include variation in the length of follow-up after SRS/SRT, limited angiographic data for all SRS/SRT patients and selection bias in both kinds of treatments.

Study results

There are currently four main strategies used for the treatment of AVMs: observation, microsurgery, embolisation and SRS/SRT.

Embolisation was developed to eliminate surgically inaccessible, deep or dural feeding arteries.[3] Embolisation may be used in isolation to other treatments but it is mainly used to reduce the size of large lesions and make previously unsuitable AVMs potential candidates for microsurgery or radiosurgery.[3]

The review found that for small, accessible lesions, excision rates for microsurgery of 94-100% (mean 98%)[3] and 98-100% (mean 99%)[7] were achieved. Microsurgery has the advantage of having a good cure rate and immediate elimination of the risk of haemorrhage.

In patients treated with SRS/SRT there is a risk of post-treatment haemorrhage in the period before complete obliteration is achieved (commonly 2-3 years). The review found that with SRS/SRT, 2 year obliteration rates of 37-85% (mean 65%) or 35-82% (mean 63%) was achieved.[7]

Harms

In studies of microsurgical treatment of small, easily accessible lesions, permanent neurological complications occurred in <5% of patients and morbidity and mortality rates were 4.6% and 0.3% respectively. For Spetzler-Martin grades IV–V, morbidity and mortality risk increased to 17.8% and 3.3% respectively.[7] When no distinction is made according to the size of lesion, one review found that for microsurgery, rates of permanent neurological complications were 1-16% and another review showed that microsurgery was associated with an 8.6% risk of morbidity and a 3.3% risk of mortality.[7]

For SRS/SRT, one review found that permanent neurological complications ranged from 1-10%.[3]

However, when considering the benefits and harms of microsurgery versus SRS/SRT, there are case-mix issues, as like is not being compared with like. Case series looking at microsurgical treatment will tend to reflect intervention in lesions amenable to surgical treatment. Where lesions are more difficult to remove, rates of effectiveness are likely to be lower.

Given the evidence base for high success rates of surgical excision in small, accessible lesions, the immediate reduction in risk of haemorrhage and the comparatively low rate of complications, microsurgery should be considered in the first instance Spetzler-Martin (SM) grading system as I-III. SRS/SRT may still be appropriate for some patients in this group.

SRS/SRT

The evidence base does not demonstrate differing levels of clinical effectiveness between the different modes of delivering SRS/SRT. The treatments are used in different contexts, with SRT commonly being utilised for the treatment of larger,

higher grade AVMs or those situated in eloquent locations.

Cost-effectiveness

There is a lack of evidence addressing the cost-effectiveness of SRS/SRT compared to other treatment options for this indication in a UK setting. However, there is some evidence from the use of SRS for other pathologies that the overall costs, including ancillary treatment and readmission costs are lower for patients treated with SRS/SRT than by microsurgery.[11] In 1997 a cost/benefit estimation for conventional fractionated radiotherapy (RT), surgery and radiosurgery (RS) for patients with single brain metastases was undertaken.[12] The cost per life year of median survivorship was $16,250 for RT alone, $13,729 for RS plus RT, and $27,523 for resection plus RT. Hence, according to this study a surgical resection resulted in a 1.8-fold increase in cost, compared to radiosurgery. A similar American comparative cost analysis found that the cost per life year gained for radiosurgery was 30% lower than for surgical resection.[13]

To date, estimates of the cost-effectiveness of SRS/SRT in comparison with surgery have not been robustly determined from a UK NHS perspective.

9. Rationale behind the policy statement

- The current evidence base for the effectiveness of SRS/SRS for the treatment of AVMs is of poor quality, consisting of case studies and case series.
- Results from case studies/series of surgical excision and SRS/SRT are difficult to compare as different interventions were applied to different patient groups.
- There is evidence of high success rates from surgical excision in small, accessible lesions and comparatively low rates of complications. Surgical excision also leads to an immediate reduction in risk of haemorrhage. However, there is no robust UK evidence for microsurgery and the national statistics show a predominance of the use of SRS for cerebral AVMs.
- Microsurgery should be considered in the first instance for emergency situations,
- In all non-emergency cases of cerebral AVMs all three modalities, microsurgery embolisation and SRS/SRT should be considered in a multidisciplinary setting.
- Given the potential associated harms of treatment, the long term risk of haemorrhage as well as the upfront risks of all interventions should be formally assessed as part of the decision process.

10. Mechanism for funding

From April 2013 the NHS CB will be responsible for commissioning in line with this policy on behalf of the population of England.

11. Audit Requirements

Audit requirements will require the following data requirements for each patient

1. Patient age
2. Location – supratentorial – superficial/deep; posterior fossa – cerebellum/brainstem
3. SM factors – size (diameter/volume), venous drainage (deep/superficial); eloquent brain (yes/no)
4. Obliteration rate – angio /MR /CT angio confirmed and time of imaging.
5. Encompassing isodose
6. Post-treatment neurological complications

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 (adult0 (subsection 4.1 Neurosurgery) stereotactic radiosurgery and stereotactic radiotherapy.

International RadioSurgery Association AVM Guidelines.

13. Links to other policies

This policy is informed by the generic NHS CB commissioning policies covering experimental treatments and the process by which individual funding requests (IFR) are handled.

14. Date of Review

3 years

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Appendix 1: Spetzler-Martin grading system

Characteristic	No. points assigned
Size	
Small (maximum diameter <3cm)	1
Medium (maximum diameter 3-6cm)	2
Large (maximum diameter >6cm)	3
Location	
Non-eloquent site	0
Sensorimotor, language or visual cortex; hypothalamus or thalamus; internal capsule; brain stem; cerebeller peduncles; cerebellar nuclei	1
Pattern of venous drainage	
Superficial only	0
Deep	1

The Spetzler-Martin scale[1] is commonly used and grades AVMs according to their size, location and type of venous drainage and the weighting for the assignment of grades is shown above. Points are allocated depending on the size, location and pattern of venous drainage and the number of points determines the grade (1 point = grade I, 2 points = grade II etc). These grades are used to inform treatment decisions, with patients of lower grade being the best candidates for surgical intervention.

Three-tier classification of cerebral arteriovenous malformations

Class	**Spetzler-Martin grade**	**Management**
A	I, II	Surgical resection
B	III	Multimodality treatment
C	IV, V	No treatment*

*Exceptions for treatment of Class C AVMs include recurrent hemorrhages, progressive neurological deficits, steal-related symptoms, and AVM-related aneurysms.

Appendix 2: Grades of evidence

evidence for clinical application

Level1 - formal, open, clinical randomised-controlled trials

Level 2 - case controlled trials (comparisons made but not randomised)

Level 3 - observational studies (including surveys and questionnaires)

Level 4 - anecdotal evidence (including independent user comments and reviews)

Level 5 - methodological verification and validation studies

Change Notice for Published Specifications and Products

developed by Clinical Reference Groups (CRG)

Amendment **to the Published Products**

Product Name	Stereotactic Radiosurgery for Cerebral Arteriovenous Malformations
Ref No	D05/P/c
CRG Lead	Stereotactic Radiosurgery

Description of changes required

Describe what was stated in original document	Describe new text in the document	Section/Paragraph to which changes apply	Describe why document change required	Changes made by	Date change made
Cerebral Arteriovenous Malformations	Stereotactic Radiosurgery for Cerebral Arteriovenous Malformations	Title page and 2nd page	To standardise naming and coding of products	Programme of Care Director for Trauma	September 2013