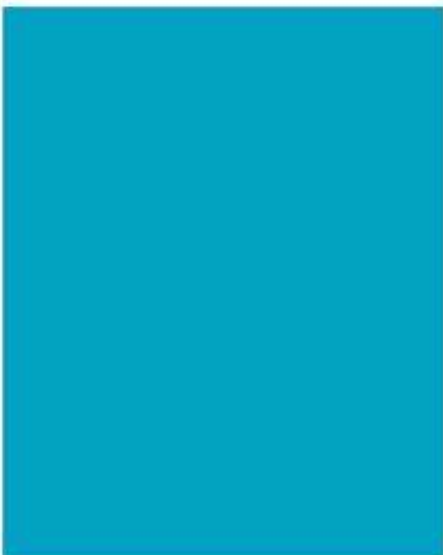


**Clinical Commissioning Policy:
Stereotactic Radiosurgery/
Radiotherapy for Glomus Tumours
(skull base paragangliomas, glomus
jugulare tumours)**

September 2013

Reference: NHS ENGLAND D05/P/f



NHS England INFORMATION READER BOX**Directorate**

Medical	Operations	Patients and Information
Nursing	Policy	Commissioning Development
Finance	Human Resources	

Publications Gateway Reference: 00407

Document Purpose	Guidance
Document Name	Clinical Commissioning Policies and Clinical Commissioning Policy Statements
Author	Various, Medical Directorate, Specialised Services
Publication Date	10 September 2013
Target Audience	NHS England Regional Directors, NHS England Area Directors, Directors of Finance
Additional Circulation List	Clinical Reference Group Chairs
Description	Production of NHS England's Clinical Commissioning Clinical Commissioning Policies and Clinical Commissioning Policy Statements
Cross Reference	N/A
Superseded Docs (if applicable)	N/A
Action Required	N/A
Timing / Deadlines (if applicable)	N/A
Contact Details for further information	Donna Hakes Medical Directorate, Specialised Services Skipton House London SE1 6LH 07785 513461 england.specialisedcommissioning@nhs.net

Document Status

This is a controlled document. Whilst this document may be printed, the electronic version posted on the intranet is the controlled copy. Any printed copies of this document are not controlled. As a controlled document, this document should not be saved onto local or network drives but should always be accessed from the intranet

NHS England

Clinical Commissioning Policy: Stereotactic Radiosurgery / Radiotherapy for Glomus Tumours (skull base paragangliomas, glomus jugulare tumours)

First published: September 2013

**Prepared by NHS England Clinical Reference Group for Stereotactic
Radiosurgery**

First published August 2013

Published by the NHS England, in electronic format only.

Contents

1. Introduction	6
2. Definitions	6
3. Aim and objectives	7
5. Evidence base.....	7
6. Rationale behind the policy statement.....	9
7. Criteria for commissioning.....	9
8. Patient pathway.....	10
9. Governance arrangements.....	11
10. Mechanism for funding.....	11
11. Audit requirements	11
12. Documents which have informed this policy.....	11
13. Links to other policies.....	12
14. Date of review	12
<i>References</i>	12

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

Glomus tumors (also known as paragangliomas or chemodectomas) are rare, benign tumors that can develop in several locations in the body including areas in and around the ear. There are two types of glomus tumors related to the ear: glomus tympanicum and glomus jugulare tumors.

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.

No high level evidence exists for any intervention (either microsurgery or SRS) in this cohort. However, from case series it is seen that radiosurgery is safe and effective. When glomus tumours are causing local mass effect on the brainstem with pressure symptoms, microsurgery is preferred.

These tumours are often extremely vascular, and they are intimately involved with the vascular structures (carotid artery, internal jugular vein) and neural structures (lower cranial nerves), which make complete resection without unacceptable side effects often predictably impossible. Previous surgery in recurrent cases would pose particular difficulties for microsurgery. The high vascularity makes them especially sensitive to radiation treatment, particularly by single fraction. Larger lesions are treated either in segments (staged) or with fractionated (hypofractionated, SRT) regimes.

It is appropriate for clinicians to consider SRS for a small subset of patients with glomus tumours 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

The basic principle of stereotactic radiosurgery (SRS) for this application is the 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. Evidence from large numbers of patients indicates that long-term tumour control is achieved in a high proportion of cases.

This policy considers the use of SRS for patients with glomus tumours and states the criteria to identify which patients should be considered for the intervention.

2. Definitions

Glomus jugulare tumours (also described as skull base paragangliomas, glomus tumours) arise from paraganglia or glomus cells in the adventitia of the jugular bulb. Glomus tumours are relatively rare (about 1 in 1.3 million people per year), usually slow-growing, hypervascular tumours. When they develop in the bony wall of the tympanic canal (glomus tympanicum) or in the middle ear, they fall into the exclusive realm of Ear Nose and Throat surgery. However, a proportion of them behave more aggressively, involving part of the skull base, in the jugular foramen and often extending up into the posterior fossa and cerebellopontine angle. These are commonly described as glomus tumours. Histologically they are nearly always considered to be benign (>99%), and metastatic spread is very uncommon – of the order of about 2%.

Glomus tumours have an incidence of 1:1.3 million, i.e. there are <50 cases diagnosed in the UK annually. They have been linked to multiple endocrine neoplasia type 2 (MEN 2), neurofibromatosis type 1 (NF1), von Hippel-Lindau disease (VHL). Less than 5% behave in a malignant manner. The female: male incidence ratio is at least 4:1. It usually presents in the 5th or 6th decade. There is no known ethnic or racial predilection. The common presentation is pulsatile tinnitus, hearing loss or hoarse voice, swallowing difficulties. More commonly occurring on the left side, multicentric tumours are found in 3-10% of sporadic cases and in 25-50% of familial cases. In these cases genetic counselling should also be advised.

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 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 specialising in the management of skull base pathologies (neurosurgeons, ENT specialists, clinical oncologists), and neuroradiologists should be involved in SRS case selection, treatment planning and delivery.

3. Aim and objectives

The clinical questions being addressed are:

- Is there sufficiently robust evidence of clinical and cost effectiveness and safety to support the use of SRS for patients with glomus tumours?
- 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

The incidence of glomus jugulare tumors is 1:1,300,000 population, providing less than 50 cases in the UK per year. The female:male incidence ratio is at least 4:1. The incidence of malignancy in glomus tumors is less than 5%.

The average age at presentation is 50 to 60 years, but this is highly variable. Catecholamine secreting (aka "functional") tumors occur in 1% - 3% of cases. There is no racial or ethnic predilection. The familial form is associated with a high incidence (25% - 50%) of multicentric paragangliomas. Multicentricity is found in about 5-15% of non-familial form patients.

5. 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.

No high level evidence exists for any intervention (either microsurgery or SRS) in this cohort. However, from case series it is seen that radiosurgery is safe and effective.

Very high morbidity and mortality is often the price to pay for total or even subtotal resectionⁱⁱ. Surgical series have often short follow up, and while mortality and major disability are reported,

Fractionated radiotherapy is effective, but due to the wide field it has been associated with bone necrosis of the skull baseⁱⁱⁱ, troublesome reduction of saliva production, brainstem radionecrosis, radiation induced stenosis of the internal carotid artery leading to hemiplegia and secondary malignancy^{iv} Reducing the radiation field

to target the circumscribed lesion rather than the surrounding tissue seemed logical, though for large tumours fractionated regimes (SRT) may be considered^v

Radiosurgery, single fraction stereotactically guided irradiation, has been introduced in the 1960s and the first publications using the technique for glomus jugulare tumours appeared in the late 1990s^{vi,vii}. Near 100% tumour control rates were achieved in most series with negligible complication rate, though long term follow up is only slowly becoming available^{viii}. It is of note that radiosurgery does not only achieve halting progression of the condition but considerable improvement in preoperative symptoms has been noted in most series, even before radiologically demonstrable shrinkage, probably due to reduction in the pulsatile compression upon the cranial nerves. Dramatic reduction in vascularity has been demonstrated on angiography.

There are few comparative studies, because surgical and radiosurgical series are often consist of different patient material^{ix}. Most radiosurgery papers report lower or negligible cranial nerve deficits that are customarily associated with microsurgery^x.

The treatment options are governed by many factors including *patient factors* (age, performance status, co-morbidity, informed patient choice), *tumour-related factors* (volume, evidence of growth) 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 or a very small tumour may appropriately lead to conservative management with a radiological surveillance programme.

Meta-analysis of 41 studies including 1310 patients showed that microsurgical cases fared worst: tumor control failure, major complication rates, and the number of cranial nerve palsies after treatment were significantly higher in surgical than in radiotherapy or radiosurgery series. Control was similar after radiotherapy and SRS, the latter about 4% better. Although the evidence is based on retrospective studies, these results suggest that surgery should be considered only for selected cases^{xi}.

SRS and SRT compared to surgery appears to provide:

- shorter hospitalisation
- a less detrimental impact on quality of life
- better short and long term morbidity
- avoidance of procedural mortality and lower treatment-related complications

Radiosurgery is preferred for tumours less than 3cm in diameter, for patients over 60 years of age and those with comorbidities: it is as effective and has lower risk of complications⁹. Similarly, post-surgical recurrences fare better with radiosurgery. Very large recurrences may require further, subtotal, surgical resection followed by radiosurgery. The expertise of the team, surgical or radiosurgical is obviously paramount.

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 in a UK setting. However, there is some evidence from other indications that the overall costs, including ancillary treatment and readmission costs are lower for patients treated with SRS than by microsurgery.^{xii} In 1997 a cost/benefit estimation for conventional fractionated radiotherapy (RT), surgery and radiosurgery (RS) for patients with single brain metastases was undertaken.^{xiii} 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.^{xiv} Given the magnitude of microsurgery for glomus tumours (much higher need for intensive care and rehabilitative service requirement than for excision of metastases in the above study) while radiosurgery is a very similar procedure for most tumours regardless of pathology, this difference and therefore the savings to the NHS by the use of SRS is likely to be even larger.

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

6. Rationale behind the policy statement

- The current evidence base regarding the effectiveness, cost effectiveness and safety of SRS/SRT for treating glomus tumours has been used as a basis for this commissioning policy.
- SRS/SRT can be used to treat glomus tumours where the relative risks of microsurgery are high, as determined by the skull base MDT.
- There is no available robust estimate of the cost effectiveness of SRS/SRT for treatment of cavernoma and ongoing monitoring of numbers and outcomes must be undertaken.

7. Criteria for commissioning

Indications for stereotactic radiosurgery/radiotherapy include newly diagnosed glomus tumours, residual tumours after previous after microsurgery and recurrent tumours.

Evidence supports the following statements:

- There is a well established role for SRS in the treatment of patients with glomus tumours
- There is a possible role for the use of fractionated RT (more than 5 fractions) in patients with large glomus tumours. Review of this evidence is beyond the remit of the SRS CRG, and lies in the province of the Radiotherapy CRG.

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

- All patients must have undergone prior assessment by the local skull base 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. In centres where there is no local SRS service, referral should be initially to the local skull base 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 glomus tumours 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 radiosurgery MDT at the stereotactic treatment centre. 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 describes 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 skull base 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 four management options for patients with glomus tumour are;

- Surgical removal (considered by the adult neurosurgery CRG)
- Stereotactic radiosurgery (SRS) or (SRT), the subject of this Policy
- Fractionated radiotherapy (considered in the radiotherapy CRG)
- No intervention

Treatment options for glomus tumours will take into consideration the precise anatomical position of the lesion, its size (dictating the perceived risk of alternative intervention with microsurgery), the presentation (clinical symptoms and signs of brain stem dysfunction necessitates surgical removal, complete or partial), and the perceived risk of microsurgery, which also informs patient choice.

The median tumour doubling rate is said to be approximately four years or longer, justifying a "watchful wait" policy for small tumours with minor symptoms in elderly patients.

Older patients have great difficulty coping with surgical complications despite the best rehabilitative efforts. The same group often present with comorbidities, questioning the wisdom of major skull base surgery. On the other hand, young

patients would have to cope for the rest of their long lives with the sequelae of surgery.

This policy does not aim to give prescriptive advice on choice of management in these cases.

All patients must be investigated for abnormal catecholamine production, for extracranial associated tumours and considered for genetic counselling and screening.

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 is 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 tumour volume, prescription dose
2. Cranial nerve status including facial nerve function and hearing before the treatment
3. MRI follow up annually for a minimum of 5 years
4. Cranial nerve status
including facial nerve function and hearing annually

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.

13. Links to other policies

This policy follows the principles set out in the ethical framework that governing 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.

References

- ⁱ Moffat DA, Hardy DG. Surgical management of large glomus jugulare tumours: infra- and trans-temporal approach. *J Laryngol Otol.* Dec 1989;103(12):1167-80
- ⁱⁱ Watkins LD, Mendoza N, Cheesman AD, Symon L. 1994. Glomus jugulare tumours: a review of 61 cases. *Acta Neurochir (Wien).* 130(1-4):66-70
- ⁱⁱⁱ Ramsden RT, Bulman CH, Lorigan BP. 1975. Osteoradionecrosis of the temporal bone. *J Laryngol Otol.* 89(9):941-55
- ^{iv} Lustig LR, Jackler RK, Lanser MJ. 1997. Radiation-induced tumors of the temporal bone. *Am J Otol.* 18(2):230-5
- ^v Krych AJ, Foote RL, Brown PD, Garces YI, Link MJ. 2006. Long-term results of irradiation for paraganglioma. *Int J Radiat Oncol Biol Phys.* 65(4):1063-6
- ^{vi} Foote RL, Coffey RJ, Gorman DA, Earle JD, Schomberg PJ, Kline RW, Schild SE. 1997 Stereotactic radiosurgery for glomus jugulare tumors: a preliminary report. *Int J Radiat Oncol Biol Phys.* 38(3):491-5.
- ^{vii} Liscák R, Vladyka V, Wowra B, Kemeny A, Forster D, Burzaco JA, Martinez R, Eustacchio S, Pendl G, Regis J, Pellet W. 1999. Gamma Knife radiosurgery of the glomus jugulare tumour - early multicentre experience. *Acta Neurochir (Wien).* 141(11):1141-6.
- ^{viii} Martin JJ, Kondziolka D, Flickinger JC, Mathieu D, Niranjan A, Lunsford LD. 2007. Cranial nerve preservation and outcomes after stereotactic radiosurgery for jugular foramen schwannomas. *Neurosurgery.* 61(1):76-81
- ^{ix} Gottfried ON, Liu JK, Couldwell WT. 2004; Comparison of radiosurgery and conventional surgery for the treatment of glomus jugulare tumors. *Neurosurg Focus* 17(2): E4
- ^x Sheehan JP, Tanaka S, Link MJ, Pollock BE, Kondziolka D, Mathieu D, Duma C, Young AB, Kaufmann AM, McBride H, Weisskopf PA, Xu Z, Kano H, Yang HC, Lunsford LD. Gamma Knife surgery for the management of glomus tumors: a multicenter study. *J Neurosurg.* 2012 Aug;117(2):246-54. doi: 10.3171/2012.4.JNS11214. Epub 2012 Jun 8
- ^{xi} Lieberson RE, Adler JR, Soltys SG, Choi C, Gibbs IC, Chang SD Stereotactic radiosurgery as the primary treatment for new and recurrent paragangliomas: is open surgical resection still the treatment of choice? *World Neurosurg.* 2012 May-Jun;77(5-6):745-61. doi: 10.1016/j.wneu.2011.03.026.

^{xii} Wellis G, Nagel R, Vollmar C, Steiger HJ. Direct costs of microsurgical management of radiosurgically amenable intracranial pathology in Germany: an analysis of meningiomas, acoustic neuromas, metastases and arteriovenous malformations of less than 3 cm in diameter. *Acta neurochirurgica* 2003;145(4): 249-55.

^{xiii} Mehta M, Noyes W, Craig B, et al. A cost-effectiveness and cost-utility analysis of radiosurgery vs. resection for single-brain metastases. *International journal of radiation oncology, biology, physics* 1997;39(2): 445-54

^{xiv} Rutigliano MJ, Lunsford LD, Kondziolka D, Strauss MJ, Khanna V, Green M. The cost effectiveness of stereotactic radiosurgery versus surgical resection in the treatment of solitary metastatic brain tumors. *Neurosurgery* 1995;37(3): 445-53; discussion 53-5.