Guidelines for the Management of Meningiomas
West Midlands Cancer Alliance

Coversheet for Cancer Alliance Expert Advisory Group Agreed Documentation

This sheet is to accompany all documentation agreed by the West Midlands Cancer Alliance Expert Advisory Groups. This will assist the Cancer Alliance to endorse the documentation and request implementation.

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<th>EAG name</th>
<th>Brain and CNS Expert Advisory Group</th>
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<tr>
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1 Introduction

The philosophy in the management of meningiomas is to treat the symptomatic or the growing tumours in order to preserve neurological function and/or to confirm diagnosis where uncertain.

Management options include:
1. Surgery
2. Radiotherapy
3. Radiological surveillance

This protocol is written to guide the management of patients with meningiomas. All cases that undergo elective treatment and selected cases that do not require active treatment should be discussed in the appropriate MDT:

1. Calvarial meningiomas at the neuro-oncology MDT
2. Skull base meningiomas at the skull base MDT
3. Spinal meningiomas are discussed on a separate section of this document.

The usual pathway for patients with meningiomas is depicted on Diagram 1.

2 Investigation for meningiomas

2.1 Brain Imaging

Patients with suspected meningioma should have standard structural MRI (defined as T2 weighted, FLAIR, DWI series and T1 pre- and post-contrast volume) as the initial diagnostic test, unless MRI is contraindicated. CT imaging should be considered if bone involvement is suspected. Specialized imaging (e.g. MRI skull base, vascular imaging, etc.) should be considered in selected cases.

2.2 Genetic testing

A minority group of patients with meningiomas have an underlying genetic disease. The best defined of these diseases is neurofibromatosis type 2. Other genetic diseases with increased meningioma risk include familial meningiomatosis, multiple endocrine neoplasia 1, Cowden syndrome, nevoid basal cell carcinoma syndrome, Werner syndrome, BAP1 tumour predisposition syndrome and Rubinstein-Taybi syndrome.¹

Suspected cases should be referred for genetic testing.

3 Treatment of meningiomas

Several factors need to be considered before deciding on offering treatment in patients with meningiomas. Patient specific factors include symptoms, neurological function, performance status, comorbidities, life expectancy and the patient’s preferences. Tumour specific factors include size and location of the tumour, perilesional oedema, surgical and radiotherapy morbidity, previous treatments.
3.1 Surgery

Surgery with the goal of maximal safe resection is the cornerstone of treatment. Indications for surgical resection include:

- Primary treatment for patients with neurological deficit and seizures.
- Primary treatment for patients with documented growth (even if asymptomatic, where the projected growth is likely to cause symptoms).
- Treatment of recurrent tumour (if deemed more appropriate to radiotherapy)
- Diagnostic or grade uncertainty

3.2 Radiotherapy

Please also refer to national NHS document on SRS/T and Proton Therapy:
https://www.england.nhs.uk/commissioning/spec-services/highly-spec-services/pbt/

3.2.1 Definitions

- Fractionated radiotherapy - delivered using image-guided intensity modulated radiotherapy (typically arc therapy)
- SRS - radiosurgery delivered in single fraction
- SRT - hypofractionated radiotherapy

Each radiotherapy departments should have guidelines and consider RCR Guidance on Target Volume Definition and Peer Review.

3.2.2 Indications for radiotherapy or SRS/T

- Recurrent or residual grade I tumours post-surgery unless further complete resection possible. (A period of observation recommended following 1st surgery unless prior documented progression.)
- Primary treatment for *inoperable tumours lacking pathological confirmation if progression at a rate consistent with benign meningioma.
- Offer fractionated radiotherapy to all grade 3 (anaplastic) meningiomas regardless of resection extent

*Inoperable: surgery associated with high risk / poor surgical candidate / unprepared to have surgery.

The role of radiotherapy for completely resected Grade 2 meningioma remains under question within Europe (ROAM study). It is reasonable to discuss on a case by case basis. If there is residual or recurrent inoperable disease radiotherapy should be discussed with the patient.

3.2.3 Relative contraindications to radiotherapy / SRS/T

- Symptomatic oedema / mass effect (consider surgery)
- Rapidly growing tumours lacking pathological verification or uncertainty in diagnosis
- *Fractionated radiotherapy is preferred over SRS/T for lesions >10cc, grade II pathology and lesions in close proximity to optic pathways

*These are relative and individual cases considered for SRS/T should be discussed within an MDT with SRS/T expertise. For example, grading for meningioma remains controversial and growth
3.3 Systemic Therapy

Currently, there are not any chemotherapeutic or other systemic agents recommended for the treatment of meningiomas.

4 Radiological surveillance for meningiomas

Meningiomas can grow slowly, intermittently or grow to a certain size and stop. Factors that predict growth are young age, hyperintensity on T2-weighted MRI and absence of calcification.\(^1\),\(^2\)

Patients with incidental and asymptomatic meningiomas that do not require treatment should have an MRI scan at 1 year and if the tumour remains stable, then the patient could be either discharged or offered a scan at 5 years (Table 1), as per NICE guideline [NG99].\(^4\)

Patient and tumour specific factors should be considered and, in some cases, regular clinical review can be offered for patients with meningioma to assess changes in their physical, psychological and cognitive wellbeing. Patients should be informed of potential new or changing neurological symptoms or signs that may occur in the future.

As meningiomas are often slow growing, serial imaging during surveillance should be compared to an initial or post-treatment baseline scan, in order to detect subtle growth over time. If the tumour grows during radiological surveillance, treatment should be considered.

5 Follow-up of meningiomas

Active monitoring of treated meningiomas aims to identify recurrent or growth of residual disease early, before the occurrence of symptoms, and inform further management. It also provides information about the course of the disease and prognosis.

The grade of the meningioma and the extent of resection are the two main predictors of long-term tumour control. Table 1 shows a possible regular clinical review schedule for people with meningioma depending on the tumour grade, as per NICE guideline [NG99].\(^4\)

If the tumour recurs or the residuum grows during radiological surveillance, treatment should be considered.

6 Specific subgroups

6.1 Radiation induced meningiomas

Radiotherapy is the only known environmental factor that is associated with an increased risk of developing meningiomas. Radiation-induced meningiomas have a more aggressive clinical behaviour and are more often multiple compared to sporadic tumours. The latency period between radiotherapy and the onset of meningiomas can be many years and therefore a longer follow-up period is required, to monitor for relapse and for secondary tumours.\(^5\)
6.2 Multiple meningiomas

A significant proportion of multiple meningiomas are asymptomatic, probably because the majority are small. The management strategy of patients with multiple meningiomas is similar to patients with a single meningioma, i.e. surveillance for stable and asymptomatic meningiomas and treatment for those that are symptomatic or growing. Radiation-induced multiple meningiomas require longer follow-up.6

6.3 Neurofibromatosis type II: NF2

All patients with NF2 should be managed with the support of the national NF2 service (Manchester or Cambridge MDT). Multiple meningiomas account for only 5% of patients with meningioma and at least 20% of these have NF2 therefore referral for genetic evaluation should be considered unless there is a known underlying cause such as previous radiotherapy7. The risk is highest in younger patients and patients under 20 with a single meningioma should also be referred for testing (personal communication with NF2 team Cambridge).

Current diagnostic criteria for NF2 are below8
  1. Bilateral vestibular schwannomas <70 OR
  2. First-degree relative family history of NF2 AND unilateral VS <70 OR
  3. First-degree relative family history of NF2 OR unilateral VS AND 2 of: meningioma, cataract, ependymoma, schwannoma, cerebral calcification (if UVS + ≥2 nonintradermal schwannomas need negative LZTR1 test), OR
  4. Multiple meningiomas (2 or more) AND 2 of: unilateral VS, cataract, ependymoma, schwannoma, cerebral calcification, OR
  5. Constitutional pathogenic NF2 gene variant in blood or identical in two tumours

6.4 Spinal meningiomas

The philosophy in the management of spinal meningiomas is similar to the cranial lesions. Patient and tumour specific factors should be considered. Elective cases should be discussed at the spinal MDT and/or neuro-oncology MDT based on local arrangements.

6.3.1 Investigations

A patient with a spinal meningioma should undergo MRI of whole neuro-axis (brain and whole spine) to assess for further lesions.

6.3.2 Treatment

6.3.2.1 Surgery
The goal of surgery is maximal safe resection. Indications for surgery include:

- Neurological deficit
- Lesions with potential for neurological deterioration
- Growth on serial imaging

6.3.2.2 Radiotherapy and Chemotherapy
Please refer to section 3.2 and 3.3
6.3.3 Surveillance

6.3.3.1 Following surgery
An initial post-operative scan should be performed to assess the extent of resection and serve for future comparison. For completely resected tumours, annual surveillance for a period of 5 years should be considered. If no growth is detected over this period, then consideration can be given to discharging the patient from routine surveillance, and further scans only performed if neurological symptoms develop. For incompletely resected tumours the period of surveillance can be extended, as per the surgeon’s clinical judgement.

If recurrence or growth is detected, then further treatment or surveillance options should be considered as appropriate.

6.3.3.2 Radiological surveillance for non-treated meningiomas
Patients with spinal meningiomas that do not require treatment should undergo annual surveillance for a period of 5 years and if no growth is detected over this period, then consideration can be given to discharging the patient from routine surveillance and further scans only performed if neurological symptoms develop.

6.4 Optic nerve sheath meningiomas
Optic nerve sheath meningiomas should be discussed at the skull base MDT. In contrast to conventional oncology principles, biopsy in suspected optic nerve sheath meningiomas is contraindicated, because it leads to poorer long-term tumour control and primary radiotherapy should be considered as the first line treatment.

6.5 Small calcified meningiomas and small dural-based lesion of indeterminate nature
Small calcified meningiomas are often found incidentally. In addition, there are multiple neoplastic and non-neoplastic lesions that radiologically mimic meningiomas. The widespread use of neuro-imaging has led to the identification on many scans of small calcified meningiomas and small dural-based lesion of indeterminate nature, which are referred to our service for expert advice. The vast majority are incidental and asymptomatic and do not require MDT discussion or clinic consultation with a Neurosurgeon. Generic advice to the referring physician could be to repeat the same modality imaging in one year and to re-refer if there is radiological change. If radiologically stable, a repeat scan should be performed when neurological symptoms/signs develop.

Patients with history of malignancy warrant discussion at the neuro-oncology MDT/ expert input, as these lesions may represent metastasis.

Enostoses (or bone islands) are small areas of compact bone within the cancellous bone that can resemble meningiomas and are sometimes seen as an incidental finding on CT scans. They do not require follow-up.

7 MDT Streamlining
A standard treatment protocol (or Standard of Care) is a point in the pathway of patient management where there is a recognised intervention that should be made available to a patient and the case should be listed, but not discussed at the full MDT meeting. Standard of Care for patients with meningiomas and potential pathways can develop for those patients that do not require surgery or radiotherapy and could be listed on the “protocol” section of the MDT list to be followed as per paragraph 3 on “Radiological surveillance for meningiomas”. Streamlining the MDT meeting will
ensure that valuable diagnostic and clinical time is used most effectively, will help to ensure there is adequate time for discussion of complex cases and will increase the transparency and consistency of care.10

For patients to be listed on the “protocol” section the following conditions must be met:

• They have been assessed by a core MDT member
• The minimum core data requirements have been met (e.g. performance status, co-morbidities etc.)
• Images have been reported by a Neuro-radiologist and all other tests relevant to the decision-making have been completed.
• Patient preference (if known) does not contradict the Standard of Care pathway.
• The Standard of Care has been reviewed by an appropriate person or triage group, there is clarity that it is appropriate, and all of the above have been fulfilled.

Where imaging is outsourced or the report has been delayed or carried out by Radiologists who are not Neuro-radiologists, the case should not be listed for discussion at the MDT in order to obtain a radiology report. The responsible clinician should seek neuro-radiology input outside the meeting first and list the patient accordingly.

The MDTs should endeavour to develop Standards of Care as a useful tool to support pathway improvement for patients and optimise use of clinical time.
Diagram 1. Pathway of patients with meningioma.

Table 1. Possible regular clinical review schedule for patients with meningioma.

<table>
<thead>
<tr>
<th>Years after treatment</th>
<th>0 to 1</th>
<th>1 to 2</th>
<th>2 to 3</th>
<th>3 to 4</th>
<th>4 to 5</th>
<th>5 to 6</th>
<th>6 to 7</th>
<th>7 to 8</th>
<th>8 to 9</th>
<th>&gt;9 (for the rest of life)</th>
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<tbody>
<tr>
<td><strong>Grade I: no residual tumour</strong></td>
<td>Scan at 3 months</td>
<td>Annually</td>
<td>Once every 2 years</td>
<td>Consider discharge</td>
<td></td>
<td></td>
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<tr>
<td><strong>Grade I: residual tumour</strong></td>
<td>Scan at 3 months</td>
<td>Annually</td>
<td>Once every 2 years</td>
<td>Consider discharge</td>
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<tr>
<td><strong>Grade I: after radiotherapy</strong></td>
<td>Scan at 6 months after radiotherapy</td>
<td>Annually</td>
<td>Once every 2 years</td>
<td>Consider discharge</td>
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<tr>
<td><strong>Grade II</strong></td>
<td>Scan at 3 months, then 6 to 12 months later</td>
<td>Annually</td>
<td>Once every 2 years</td>
<td>Consider discharge</td>
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<tr>
<td><strong>Grade III</strong></td>
<td>Every 3 to 6 months</td>
<td>Every 6 to 12 months</td>
<td>Annually</td>
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<tr>
<td><strong>Asymptomatic incidental meningioma</strong></td>
<td>Scan at 12 months. If no change consider discharge or scan at 5 years.</td>
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* The presence of any residual tumour can only be established after the first scan at 3 months.
References

4. Brain tumours (primary) and brain metastases in adults NICE guideline [NG99] Published date: July 2018. [https://www.nice.org.uk/guidance/ng99](https://www.nice.org.uk/guidance/ng99)