

**EAST MIDLANDS
Brain & CNS Expert Clinical Advisory Group**

**Guidelines for the Investigation and Treatment of
Brain and CNS Cancer
(Including Operational Framework)**

(Demonstrating Compliance with Measure 10-1C-103k)

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Contents	Page
Summary of Operational Arrangements	3
1.0 Presentation Pathway	
1.1 Referral Arrangements	5
1.2 Protocol for Emergency Surgical Arrangements	7
1.3 Referral Guidelines Between Teams	7
2.0 Diagnostic Pathway	8
2.1 Diagnosis and Imaging	8
2.2 Diagnosis and Pathology	13
3.0 Treatment Pathway	
3.1 Surgical Management of Patients	14
3.2 Oncology	18
3.3 Palliative Care	21
3.4 Rehabilitation	22
4.0 Follow up Pathway	23
Teenage and Young Adult Pathways	22
5.0 Treatment of Brain Metastases	23
Appendix 1: Patient Pathway	25
Appendix 2: WHO grading scheme	27
Appendix 3: Cerebral Metastases Policy	29

Page Reference Number for Peer Review Measures

Measure	Page Number
11-1C-105k	5
11-1C-106k	8
11-1C-107k	14
11-1C-108k	23
11-1C-110k	7
11-1C-117K	22
11-1C-118k	22

Summary of Operational Arrangements

The arrangements for the diagnosis and treatment of people with brain and other CNS tumours are governed by the NICE Improving Outcomes Guidance published in June, 2006. The key principles from this document have been adopted by the Neuro-oncology Services as the Operational Framework within the East Midlands Cancer Network as follows:

- Within the EMCN the care of all patients with brain and other central nervous system (CNS) tumours will be coordinated through multidisciplinary assessment and care. For the majority of EMCN this tertiary provision is through the Neuro-sciences Services at Nottingham University Hospitals NHS Trust. For the south of the EMCN (Northamptonshire) this tertiary service is provided by Oxford Radcliffe Hospitals NHS Trust.
- Each Acute Trust within the EMCN has designated a neuro-oncology clinical lead
- The EMCN has developed a model of Network Local MDTs to support the ongoing care of patients and their families as close to home as is safe and practical
- The Key Worker Policy has been developed and agreed
- EMCN supported upgrade VTC on an N3 platform, MoVi and the roll out of APC to facilitate image sharing and consultation both within and out of hours to ensure that every patient with imaging that suggests a diagnosis of CNS tumour is discussed by the neuroscience brain and other CNS tumours MDT without delay. This is to ensure that radiological diagnosis is confirmed and advice on further management can be given, regardless of the source of the initial referral or possible need for specialist treatment.
- Neuropathology reports to the standards defined by the Royal College of Pathologists (Code of practice for histopathologists and histopathology services, Royal College of Pathologists – section 22 – 2010)
http://www.rcpath.org/resources/pdf/g030codeofpracticehisto2009_jan10.pdf
- Neuroradiologists report and review examinations to the standards defined by the Royal College of Radiologists.
- There is ready access to a neurosurgical biopsy or resection service, including image localisation and stereotactic techniques through the designated Neurosciences Services
- Preoperative discussions should take place at the neuroscience brain and other CNS tumours MDT to determine the optimum approach to surgery and the processing of tissue specimens, including intraoperative histological evaluation.
- An intraoperative histopathological diagnostic service is available to support surgical interventions with clear procedures in place to inform the clinical team of arrangements for out-of-hours requirement for an intraoperative opinion in non-elective cases. Either smear preparations or frozen sections may be used. In the current imaging era the evidence base for the benefit of the technique is very limited and its use in diagnosis varies accord.
- Final diagnosis, treatment planning and patient counselling is based on the final report of the paraffin histology.

- Specialist neuropathology should include autopsy facilities to support both consented and Coroner's examinations such that feedback can be obtained on any post-operative deaths or deaths while on treatment wherever they occur in the Network. In the case of Coroner's autopsies systems should be in place to ensure that relatives are given the opportunity to request formal neuropathological examination in appropriate cases. There should be provision of a post mortem brain examination service to receive material for a clinical diagnostic opinion from local autopsies (authorised by H.M. Coroner or with consent from relatives) as well as referred cases from elsewhere in the Network. Material may include whole brain, whole spinal cord, peripheral nerve. Large or small block samples and slides may also be received for clinical opinion. Neuropathologists provide a network service based on one clinical neuroscience centre. They should have time to give clinical advice to colleagues in the network as to the extent of examination and requirements for tissue retention in relation to the neuropathological component of examinations performed in other centres. Information from post mortem examinations should be integrated into regular mortality meeting reviews carried out by the MDT team.
- Healthcare professions have face-to-face communication with patients, their relatives and carers at critical points in the care pathway to discuss diagnosis, prognosis, treatment options (including no treatment), recurrence and end-of-life care. Clear, high-quality and relevant written information material should be made available to support patients, their relatives, carers and professionals in this process.
- There is a bereavement service in the Trusts providing services to CNS tumours to assist families in the event of a death
- Clinical nurse specialists are core members of the neuroscience brain and other CNS tumours MDT and the cancer network brain and other CNS tumours MDTs and may need to work across several geographical sites. They are likely to take on the role of key worker for many patients, especially during the early stages of their clinical care, providing supportive care, information and continuity of care with other healthcare professions.
- There should be ready access to specialist neuropsychology and neuropsychiatry services for assessment and management of complex cognitive, emotional and behavioural problems. This is an area of development.
- There should also be access to specialist healthcare professions as appropriate for any other problems patients may experience, such as epilepsy, headaches and functional loss, for example, speech, language or visual problems.
- Palliative care specialists should be included as members of the neuroscience brain and other CNS tumours MDT and the cancer network MDTs.
- There should be rapid access to allied health professional assessment and rehabilitation services, including specialist neurorehabilitation when appropriate as a patient's condition changes.
- There should be immediate access to specialist equipment as necessary.
- Data collection system is in place for information on all patients with a radiologically or histopathologically confirmed CNS tumour.
- Entry into clinical trials is fully supported

1.0 Presentation Pathway

1.1 Referral Arrangements

(Demonstrating Compliance with Measure 11-11C-105k) – The Presentation Pathway)

Patient Pathway attached as **Appendix 1**.

The referral arrangements for patients with suspected brain and CNS cancer cover both newly presenting patients and patients presenting with symptoms suggestive of recurrence.

It includes referral from Primary Care and also from other hospital doctors (who are not members of a brain and CNS MDT or part of the diagnostic service)

Referral arrangements - General Points:

A patient should be referred who presents with symptoms suggestive of brain or CNS cancer to an appropriate specialist.

- Discuss any concerns about a patient's symptoms and/or signs with the local specialist
- If rapid access to scanning is available, consider as an alternative to referral
- Reassessment and re-examination if the patient does not progress according to expectations.

Urgent referral:

Refer urgently patients with:

- Symptoms related to the CNS, including:
 - Progressive neurological deficit
 - New-onset seizures
 - Headaches
 - Mental changes
 - Cranial nerve palsy
 - Unilateral sensorineural deafnessin whom a brain tumour is suspected
- Headaches of recent onset accompanied by features suggestive of raised intracranial pressure, for example:
 - Vomiting
 - Drowsiness
 - Posture-related headache
 - Pulse-synchronous tinnitus
- Other focal or non-focal neurological symptoms, for example blackout, change in personality or memory
- A new, qualitatively different, unexplained headache that becomes progressively severe
- Suspected recent-onset seizures (refer to neurologist).

Consider urgent referral (to an appropriate specialist) in patients with rapid progression of:

- Subacute focal neurological deficit
- Unexplained cognitive impairment, behavioural disturbance or slowness, or a combination of these

- Personality changes confirmed by a witness and for which there is no reasonable explanation even in the absence of other symptoms and signs of a brain tumour

Non-urgent referral:

Consider non-urgent referral or discussion with specialist for:

- Unexplained headaches of recent onset:
 - Present for at least 1 month
 - Not accompanied by features suggestive of raised intracranial pressure

Suspected Cerebral Metastases

Refer urgently patients previously diagnosed with any cancer who develop any of the following symptoms:

- Recent-onset seizure
- Progressive neurological deficit
- Persistent headaches
- New mental or cognitive changes
- New neurological signs

Investigations:

- In a patient with new, unexplained headaches or neurological symptoms, undertake a neurological examination guided by the symptoms, but including examination for papilloedema. (Note that the absence of papilloedema does not exclude the possibility of a brain tumour).
- When a patient presents with seizure, take a detailed history from the patient and an eyewitness to the event. Carry out a physical examination, including cardiac, neurological and mental state, and developmental assessment, where appropriate.

Recurrence:

The contact points for primary care to refer back patients with symptoms suspicious of recurrence are the 2ww office or equivalent in each Trust (see box below with details).

The PCT agreed point of contact for Referral for Suspected Cancer has been agreed as the 2ww office or equivalent in each Trust. This policy was reconfirmed by the PCT representatives at the EMCN Board on 21.07.09.

Trust	Named Contact	Telephone/email
Kettering General Hospital NHS Foundation Trust (KGH)	2ww Office	01536 493303
Northampton General Hospital NHS Trust (NGH)	2ww Office	01604 544235
University Hospitals of Leicester NHS Trust (UHL)	Cancer Office	0116 250 2543
Derby Hospitals NHS Foundation Trust (DHFT)	Via Choose & Book or Gynaecology Clinic	Direct Fax 01332 789157
Burton Hospitals Foundation Trust (BHFT)	Patient Access Centre	Direct Fax 01283 593090

Sherwood Forest Hospitals NHS Foundation Trust (SFHT)	Choose and Book	01623 622515 Ext 4015
Nottingham University Hospitals NHS Trust (NUH)	Helen Andrews	0115 9691169 Ext 57964
United Lincolnshire Hospital NHS Trust (ULHT)	Julie Miller (Appointments Team Leader)	01522 573738 Fax:- 01522 573351 2WeekWaitTeamLincoln@ulh.nhs.uk

1.2 Protocol for Emergency Surgical Interventions

(Demonstrating Compliance with Measure 11-1C-110k)

1. Until management has been formally taken over by a core member of the Brain and CNS MDT patients needing emergency surgery for a CNS tumour will remain under the care of the admitting Consultant/duty Consultant Neurosurgeon of the week.
2. Patients presenting as an emergency will be stabilised and then transferred to the relevant specialist team.
3. Every possible effort is made by a non core member of the CNS MDT responsible for the emergency management of a patient with a CNS neoplasm to endeavour to have informed a core surgical member of the CNS MDT, of such a clinical scenario at the earliest opportunity.
4. Where possible this discussion should take place within the forum of a clinical radiology meeting.
5. The purpose of this discussion is to endeavour (where possible) for a core surgical member of the CNS MDT to take over management from that point onwards.
6. Alternatively, with the agreement of a core surgical member of the CNS MDT surgical management is agreed with a non core CNS MDT neurosurgeon. This must be documented in the patient record.
7. This decision process is to be noted at formal post surgical review at the CNS MDT (for audit purposes).

This policy has been circulated through the Trust Teams and Directorates.

1.3 Referral Guidelines Between Teams

Tertiary Referrals:

Referrals to the tertiary centre at NUH from other trusts within the East Midlands Cancer Network were agreed in August 2005.

Tertiary referrals are received from a wide area with an estimated population of 4.2 million. This covers Nottinghamshire, Lincolnshire, Derby City and parts of Derbyshire County, the Burton area of South Staffordshire, Leicestershire and Rutland.

Tertiary referrals from Northamptonshire are to Oxford as per the agreed pathway.

General Criteria for Referral

- ALL adult patients with suspected Primary Brain and other CNS tumours should be referred to the Neuro-oncology MDT for discussion
- Patients under 16 years of age from across the entire EMCN should be referred to the EM Paediatric Service through the hub at Nottingham University Hospitals

2.0 The Diagnostic Pathway **(Demonstrating Compliance with Measure 11-1C106k)**

Patient pathway attached as **Appendix 1**.

Prior to referral to the neurosurgeons at the Neuroscience Centre in Nottingham all patients whether it is a new diagnosis, a suspected recurrence or an unexpected imaging diagnosis of CNS tumour should have an initial diagnostic test which should be:

1. CT scan completed which indicates a positive diagnosis of brain cancer
OR
2. MRI scan completed which indicates a positive diagnosis of brain cancer

The main aims of imaging of brain tumours are:-

- Primarily diagnose or refine a suspected diagnosis
- Optimally localise the lesion
- Characterise the lesion
- Assess the lesion's secondary effects and complications
- Plan surgical and radiation treatment including provision of input data for neuronavigation
- Recognise post-treatment progress and complications

Where possible the following protocols should be adhered to:

- All CT and MRI brain scans should be reported on by a neuro-radiologist
- Ideally, all scans performed outside the neurosciences centre should be reviewed by the neuroradiological team prior to treatment

All diagnostic imaging suggestive of primary CNS tumours should be referred to the NSMDT within 2 working days.

2.1 Diagnosis and Imaging

Brain Primary Tumours

Who should be imaged?

All patients suspected of having a primary brain tumour should be imaged initially with MRI or CT.

Imaging objectives

- To detect tumour.
- To characterise tumour.
- To determine extent of tumour.
- To select optimal site for obtaining histological material (preferably where tumour grade is highest and avoiding eloquent areas and those with a large amount of necrosis or not cyst formation).

MRI is the investigation of choice in the evaluation of primary cerebral neoplasms. It is superior to CT for tumour detection due to better contrast resolution, which gives a high sensitivity to any alteration in the nature of brain tissue. However, CT can provide unique information not readily available on MRI (e.g. the presence of calcification) and is still used in

the primary investigation of non-specific neurological presentations, which may occasionally be caused by the tumour. If a mass-like lesion is detected on CT, MRI should be undertaken for further characterisation and to assess the full extent of disease. Nevertheless, MRI is unable to predict tumour type and histological grade reliably. Signal intensity and contrast enhancement characteristics may assist the surgeon in choosing a site for biopsy and imaging may be used for guiding stereotactic biopsy procedures. Proton MR Spectroscopy (¹H-MRS), single photon emission computed tomography (SPECT) and positron emission tomography (PET) remain experimental procedures in the evaluation of brain tumours. High resolution CT is useful in addition to MRI in pre-operative assessment and follow up of skull base tumours.

Imaging should be able to discriminate between tumours and other intracranial mass lesions, e.g. infarcts, haemorrhage or inflammatory/demyelinating lesions. Some tumours have characteristic features on imaging which allow a definite diagnosis to be reached prior to biopsy. However, most tumours will need to be biopsied for histological classification.

Unlike tumours elsewhere in the body a biopsy is not usually obtained prior to definitive surgery. Intra-operative histological evaluation by a specialist neuropathologist is, however, commonly obtained. A decision will be made on imaging as to whether image-guided, open biopsy or resection is most appropriate for patient management. In some instances, it will be decided that biopsy is neither feasible nor clinically appropriate. Depending on the presumed diagnosis, these patients may have surveillance follow up imaging or referral for palliative radiotherapy.

Imaging - MRI

For the majority of supratentorial tumours conventional MR imaging is undertaken with the use of intravenous contrast medium enhancement using a low molecular weight, extracellular gadolinium containing contrast agent such as Gd-DTPA. As 70% of adult brain tumours are supratentorial the following technique is advised.

Protocol for imaging of adult brain tumours			
Sequence	Plane	Slice thickness	Field of view
T2W	Axial	5 ± 1mm	Whole brain
FLAIR*	Axial + Coronal	5 ± 1mm	Whole brain
T1W	Coronal/Axial	5 ± 1mm	Whole brain
T1W with contrast medium enhancement		6 ± 1mm	Whole brain

*Fluid attenuated inversion recovery

Surgeons usually like at least one sequence in the sagittal plane in addition to the above to aid in surgical planning. Diffusion-weighted imaging (DWI) is of value in discriminating between infarcts and tumours and abscesses and necrotic or cystic tumours.

Variations to the standard “brain” protocol are necessary for investigation of parasellar tumours and tumours of the cerebellopontine angle, such as acoustic schwannomas.

In the paediatric population a higher percentage of tumours (around 50%) are located in the posterior fossa. Sagittal imaging can be useful in assessment of medulloblastoma and other midline tumours such as pineoblastomas and germ cell tumours which tend to occur in younger patients.

Pre-operative MRI of the whole spine to look for meningeal “drop” metastases is essential in paediatric patients with tumours of the posterior fossa or pineal gland.

Protocol for imaging of adult brain tumours			
Sequence	Plane	Slice thickness	Field of view
T1 pre- and post-contrast medium	Sagittal	3 ± 1mm	Large
T1 pre- and post-contrast medium	Axial where abnormal	4 ± 1mm	Small

Imaging - CT

- 1-5mm axial sections using spiral techniques from the skull base to the vertex, parallel to the clivus to avoid irradiation of the orbits.
- Scans should be obtained pre- and post-injection of 50-100ml of intravenous contrast medium.
- Using MDCT slice thickness will depend on scanner capability. In general, sections are acquired at 1.25-2.5mm and reformatted at 5mm for viewing.

Values of CTDI_{vol} should normally be below the relevant national reference dose for the region of scan and patient group.

Immediate pre- and intra-operative imaging

Both CT and MRI are used for directing image-guided biopsy. This will be performed in dedicated neurosurgical units. Additional sequences that aid in surgical planning may need to be performed. These will include DWI, MR angiography (MRA), MR venography (MRV) and CT angiography (CTA). MRS, SPECT and PET are techniques that may help in identifying the area of highest grade of malignancy and, thus influence choice of biopsy site.

Follow up

Patients may be treated by complete or partial resection, radiotherapy, chemotherapy or by adopting a wait and watch policy. The requirement for follow up imaging of different CNS tumours is variable and the Neuroscience and Cancer Network MDT will usually determine follow up protocols.

In obtaining any follow up imaging, care should be taken to obtain sequences in an identical manner to previous investigations including the same scanning plane (including angle), slice thickness and sequence type.

Following surgery meningeal enhancement is frequently seen and may last for years. Enhancement of the parenchyma adjacent to the resection cavity usually appears within the first 24 hours but resolves in 6-12 months. It is seen earlier and more clearly on MR imaging than on CT. A variety of changes, including white matter signal abnormality, may be seen following radiotherapy. Since the incidence of recurrence of brain tumours is high, it is useful to have a post-treatment baseline scan approximately 3 months after completion of therapy. Further imaging is indicated when new symptoms develop. Paediatric tumours are commonly scanned within 24 hours of surgery to assess the extent of residual disease.

Follow up of gliomas is variable and depends on the underlying histology, patient symptoms and the nature and extent of treatment undertaken. Prolonged survival with low grade glioma should use the same protocols as at diagnosis. Follow up scans are performed at intervals as determined by the local MDT.

Acoustic neuromas and pituitary tumours are other examples of tumours which may require long term imaging follow up.

Protocol for imaging of acoustic neuromas			
Sequence	Plane	Slice thickness	Field of view
T2W	Axial/Coronal	5 + 1mm	Whole brain
T2W	Axial /Coronal	3 ± 0.3mm	Small
T1W	Axial	3 ± 0.3mm	Small
T1W with contrast medium enhancement	Axial	3 ± 0.3mm	Small

When screening for possible acoustic neuroma 3-D volume T2W sequences such as CISS (constructive interference in the steady state) or DRIVE (driven equilibrium radio frequency reset pulse) are usually sufficient).

Acoustic neuromas are commonly managed with surveillance scanning. Volume T2W using sequences described above is usually sufficient but post-contrast T1 in the axial and coronal planes may be performed. Post operative follow up of acoustic neuromas does require a contrast medium enhanced scan to detect nodular areas of recurrence. Linear enhancement of the internal auditory meatus (IAM) and adjacent is a normal post-surgical finding.

Protocol for imaging of pituitary or parasellar tumours			
Sequence	Plane	Slice thickness	Field of view
T2W/FLAIR	Axial	5 + 1mm	Whole brain
T1W	Sagittal & Coronal	3 ± 0.3mm	Small
T2W	Coronal	3 ± 0.3mm	Small

Enhancement with gadolinium is not recommended for routine use in the investigation of pituitary microadenoma. In Cushing's, growth hormone deficiency or diabetes insipidus contrast medium enhancement is required. On the first examination of a presumed pituitary macroadenoma, contrast medium enhancement will be helpful to discriminate between other sellar or suprasellar tumours e.g. craniopharyngiomas or meningiomas.

Follow up imaging of histologically verified pituitary macroadenomas does not normally require contrast medium enhancement. A baseline scan should be obtained at 4-6 months post surgery as reduction in size of any residual soft tissue within the sella occurs during that time.

Tips

- The TNM system is not useful for primary brain tumours.
- Histology of tumour is by far the most important prognostic factor.
- MRI should be able to discriminate between tumours and other intracranial lesions.
- Following treatment, meningeal enhancement may be prolonged and should be interpreted with caution.
- Pre-contrast CT may demonstrate calcification and haemorrhage frequently obscured on post-contrast scans.

Brain Metastases

Clinical Background

All malignant tumours can metastasise to brain with lung, breast and melanoma doing so most frequently. Brain metastases from gastrointestinal (GI) and genitourinary tract (GU) tumours occur less commonly. The majority of metastases (80%) are supratentorial. However, GI and GU tumour metastases are more common in the posterior fossa, 50%

being infratentorial. Within the cerebral hemispheres the grey/white matter junction is the most common site of metastases. Diagnosis is usually made on the basis of multiple lesions but solitary brain metastases occur and may be resectable. Multiple lesions are treated with chemotherapy which will include the use of corticosteroids or radiotherapy which may be to whole brain or to individual lesions (stereotactic external beam radiotherapy or gamma knife irradiation). Metastases are usually of high signal intensity on T2W imaging and of intermediate signal intensity on T1W imaging, although this signal pattern is sometimes reversed in haemorrhagic metastases, and mucinous adenocarcinoma. There is usually surrounding oedema and the degree may be variable but it is often disproportionate to the size of the lesion. Metastases situated in the grey matter tend to be associated with less oedema than those found in the white matter. Enhancement with contrast medium is typical and may be seen throughout the lesion or only at its rim.

Meningeal metastatic disease is diagnosed by the presence of multiple enhancing nodules in the leptomeninges. Dural enhancement may be normal within the cranial cavity particularly after a CSF tap. Meningeal metastatic disease may be present in the absence of meningeal enhancement and confirmed by cytology even when MRI is entirely normal. Conversely, no malignant cells may be found on cytology despite abnormal meningeal enhancement.

Who should be imaged?

All patients with a previous history of malignancy and symptoms or signs suggesting metastatic disease to the brain should be imaged initially with MRI or CT

Imaging objectives

- To detect the presence of brain metastases.
- To identify the number of metastases.
- To determine tumour extent

Protocol for imaging of brain metastases			
Sequence	Plane	Slice thickness	Field of view
T2W	Axial	5 ± 1mm	Whole brain
FLAIR	Axial	5 ± 1mm	Whole brain
T1W	Axial	5 ± 1mm	Whole brain
T1W with contrast medium	Axial/Coronal	5 ± 1mm	Whole brain

The dose of gadolinium containing contrast medium given may vary with therapeutic intent. Normal 0.1 mmol/kg patient body weight of Gd-DTPA is given (or equivalent, if contrast agents of higher relaxivity are used) but this may be increased to increase the sensitivity. Higher doses may be used if resection or targeted irradiation is being contemplated.

CT

- 1-5mm axial sections using spiral techniques from the skull base to the vertex, parallel to the clivus to avoid irradiation of the orbits.
- Scans should be obtained pre- and post-injection of 50-100 ml of intravenous contrast medium.
- Using MDCT slice thickness will depend on scanner capability. In general, sections are acquired at 1.25-2 mm and reformatted at 5mm for viewing.

Values of CTDI_{vol} should normally be below the relevant national reference dose for the region of scan and patient group.

PET-CT

Although intracranial metastases may show uptake with ^{18}F FDG, PET-CT is not generally used for intracranial lesion detection because grey matter demonstrates (normal) physiological uptake of this tracer.

Follow up

After resection/targeted radiotherapy of a solitary metastasis or whole brain radiotherapy for multiple brain metastases follow up MRI may be performed after completion of treatment to serve as a baseline. However, patients may also be managed expectantly and only re-imaged when new symptoms develop. Again, the imaging technique should be the same as that used at diagnosis of metastatic disease.

CT is sometimes used at diagnosis and follow up. If a firm diagnosis of multiple metastases can be made by the presence of enhancing lesions in the brain and treatment can be planned accordingly, it may not be necessary to undertake MRI at follow up. However, contrast-enhanced MRI is the most accurate available technique for establishing the site, size and number of metastatic intracranial lesions and is best for the follow up also.

Tips

- Pre-contrast CT or MRI scans are useful in patients with suspected metastases from testicular non-seminomatous germ cell tumours which are frequently haemorrhagic.
- Malignant melanoma metastases are frequently of high signal intensity on pre-contrast MRI T1W images due to the paramagnetic effects of melanin and of high density on pre-contrast CT scans.

Board of the Faculty of Clinical Radiology and Royal College of Radiologists (2005) *Cancer Multidisciplinary team meeting – standards for clinical radiologists*. London: Royal College of Radiologists. Available from: www.rcr.ac.uk

2.2 Diagnosis and Pathology

Primary tumours of the nervous system are classified and graded according to the WHO grading scheme – see **Appendix 2**.

Detailed guidance is provided in two documents published by the Royal College of Pathologists which specifies the scope of a neuropathology service and standards for reporting expected for neuro-oncology.

The Royal College of Pathologists (2008) *Minimum dataset for the histopathological reporting of tumours of the central nervous system*. London: Royal College of Pathologists. Available from:-

http://www.rcpath.org/resources/pdf/g609_cns_dataset_final_april_08.pdf

The Royal College of Pathologists (2010), *Code of practice for histopathologists and histopathology services – section 22*, London: Royal College of Pathologists, available from:- http://www.rcpath.org/resources/pdf/g030codeofpracticehisto2009_jan10.pdf

Definitive diagnosis of a brain tumour requires histological examination of representative tissue from the lesion by a qualified and experienced neuropathologist. Diagnosis based on clinical and or radiological findings alone should be viewed as presumptive and should not

form the basis for definitive treatment or further clinical management unless there are compelling clinical considerations that preclude biopsy.

Where initial diagnostic evaluation by the specialist neuropathology service indicates that a tumour is not a primary CNS tumour then the case and material will be referred to a specialist pathologist in the relevant cancer MDT in the network. Primary bone tumours other than those affecting the skull base are referred to the specialist orthopaedic pathology service in Birmingham.

Where local laboratory facilities do not offer a particular diagnostic test then material will be referred to another laboratory that has CPA accreditation.

In cases of diagnostic difficult cases will be referred for an external opinion to another UK specialist neuropathology service. The main services used are:-

- Neuropathology Section, Institute of Neurology, Queen Square, London
- Neuropathology Department, Edinburgh
- Orthopaedic pathology service, Birmingham

Cases presented at the MDT will be reviewed before the meeting by specialist neuropathology review. The purpose of this review is to check on accuracy of diagnosis and ensure that the report meets the standards specified for a minimum dataset. Where possible a pathologist other than the original reporting pathologist will undertake a review.

Intra-operative opinions will be provided where requested by the surgical team for elective cases.

The Laboratory and histopathological/histochemical investigations and their indications

http://www.rcpath.org/resources/pdf/g101_tp_non_neo_neuro_nov10.pdf

3.0 The Treatment Pathway **(Demonstrating Compliance with Measure 11-1C-107k)**

Patient pathway attached as **Appendix 1**.

The Treatment Pathway covers the process of active treatment delivery up to, but not including, referral for follow up. It covers this process whether it is with radical or palliative intent and whether it is for treatment of a first presentation or of a recurrence. It also covers the situation where the treatment plan is to offer palliative and supportive care only, rather than active tumour removal or cytoreductive therapy.

3.1 Surgical Management of Patients

Management for a particular patient will depend on multidisciplinary discussion at the MDT taking into account all relevant clinical factors but working in accord with the broad guidelines below.

Surgical Guidelines

Tumour Type	Aims of Surgery	Operation Performed
Adult High Grade Glioma	Tissue diagnosis Cytoreductions (esp if ↑ICP) Maximal resection in selected cases	Biopsy – stereo/IG or debulking as appropriate Gliadel wafers may be used if 90% or greater resection and with prior MDT agreement
<p>Rationale:- tissue diagnosis required prior to radiotherapy . Radiotherapy better tolerated if ICP addressed. <i>Improved outcome now established for greater than 90% resections on post op MRI</i></p> <p>Reoperation – Limited role – drainage of cysts, occasional further debulking ± Gliadel wafers after MDT discussion</p>		
Adult Low Grade Glioma	Tissue diagnosis Resection where feasible	Biopsy – stereo/IG Resection/Lobectomy
<p>Rationale:- detection of dedifferentiation at first opportunity possible improved prognosis with resection of polar lesions</p> <p>Reoperation – Indicated where recurrence or concerning appearances on surveillance scans/deterioration in appearances or suggestions of dedifferentiation. MDT may agree that there is good evidence of progression to higher grade without biopsy being mandatory</p>		
Meningioma	Tissue diagnosis Maximal resection ± margins	Maximal feasible resection (with involved dura and bone). Increasingly acceptable to leave limited residuum e.g. along cavernous sinus recognising a role for stereotactic radiosurgery
<p>Rationale:- recurrence correlates with extent of resection</p>		
Recurrent Meningioma		Resection if symptomatic or growth of tumour on serial imaging. Stereotactic radiosurgery in appropriate cases Reresection for atypical cases
<p>Rationale:- surgery the most effective treatment in disease control</p>		
Intracranial Metastasis	Tissue Diagnosis. Symptom control	Resection. Stereotactic radiosurgery for smaller mets in eloquent areas. Should be preceded by full staging and discussion in neuro-oncology and appropriate site specific MDT
<p>Rationale:- control symptoms and prolong survival where disease elsewhere under control</p>		
Multiple Intracranial Metastasis	Tissue diagnosis symptom control	Resection of at most 2 mets or largest metastasis

Rationale:- intracranial disease will cause more symptoms and kill patients before disease elsewhere)

Paediatric Cerebellar Pilocytic Astrocytoma	Tissue diagnosis. Possible cure.	Resection
Rationale:- resection associated with high chance of cure with surgery alone		
Residual/Recurrent Pilocytic Astrocytoma		Consider further resection taking into account reason for incomplete resection in first instance. Either re-resect or await development of symptoms
Rationale:- surgery by far the most effective treatment for this localised disease		
Paediatric post fossa Ependymoma	Tissue diagnosis Cytoreduction Symptom control	Maximal resection feasible taking into account neuraxis staging
Rationale:- pre-eminent role of surgery in disease control recognised		
Residual/Recurrent Ependymoma		Consider 2 nd look surgery for localised disease. Only if symptomatic or documented progression on scan
Rationale:- pre-eminent role of surgery in disease control recognised		
Paediatric post fossa Medulloblastoma	Tissue diagnosis Cytoreduction Symptom control	Maximal resection feasible taking into account neuraxis staging
Rationale:- Outcome improved with more extensive resection		
Pineal and Tectal Plate Lesions	Tissue diagnosis Symptoms control	Hydrocephalus treatment CSF markers first Biopsy – endoscopic or stereotactic – of small lesions Resection of larger lesions
Rationale:- diverse range of lesions requiring diverse treatments so should establish a tissue diagnosis where possible; tumour markers may obviate need		
Paediatric Brain Stem Glioma	Tissue Diagnosis?	No surgery in classic cases “radiological diagnosis” Biopsy in atypical cases
Rationale:- biopsy carries risk of complications and of sampling error in heterogeneous tumours. Dreadful prognosis		
Pituitary Macroadenoma	Preserve/improve vision	Transphenoidal surgery,

(non-functioning)	Maximal clearance of tumour	endoscope or microscope
Rationale:- adequate surgery decompresses anterior visual pathways and minimises risk of longer term recurrence		
Re-operation:- for recurrence may be considered if feasible and if considered appropriate after pituitary MDT discussion. All patients managed in conjunction with endocrinologists		
Pituitary Microadenoma (functioning)	Biochemical cure	Transphenoidal surgery, endoscope or microscope
Rationale:- to correct excess morbidity mortality with pituitary hypersecretion syndromes e.g. Cushings, acromegaly		
Re-operation:- for recurrence may be considered if feasible and if considered appropriate after pituitary MDT discussion. All patients managed in conjunction with endocrinologists		
Vestibular schwannoma	Complete tumour removal for growing tumours either when too large for radiosurgery or when patient prefers surgery	Retrosigmoid of translabarynthine surgery
Rationale- microsurgical resection offers complete tumour removal with resultant long term cure. Adie from conservative management it is the only option for large tumours and is preferred by some patients with smaller tumours.		
Management would be under a neuro-otology neurosurgical team, taking in mind non-surgical options and with skull base MDT discussion.		
Skull base tumours in general	Heterogeneous indications for surgery Tissue diagnosis Symptoms control where cure not feasible Attempt at cure with maximal resection and adjuvant treatment	Biopsy (often endoscopic) Skull base approach and debulking/maximal resection
Tissue diagnosis is always desirable due to range of possible diagnoses, more extensive surgery either as symptoms control strategy or as curative strategy considered within head and neck MDT or skull base MDT		

SPINAL TUMOURS

Tumour Type	Aims of Surgery	Operation Performed
Extradural	Symptom Control Tissue Diagnosis	Neurological decompression Bony stabilisation – INST Bony support - PLASTYS
Overlap with MSCC Orthopaedic Spinal Surgery		
Intradural	Symptom Control Tissue Diagnosis Cure	Minimal bony resection Complete Resection where possible Curative Surgery
Complete resection expected to be curative except syndromic or residual disease		
Intramedullary	Symptom Control Tissue Diagnosis	Decompressive bony resection ± dural expansion ± fusion

	Cytoreduction Possible Cure	Debulking to complete resection where possible Biopsy if no plane/unsafe
Tissue diagnosis often difficult by radiology/interoperative histology: extent of resection determined by presence of distinct tumour/interoperative plan of dissection		
NF2	Symptom Control Tissue Diagnosis Cyto Reduction	Maximal resection depending on site of tumours etc.
Genjomic Syndrome Overlap with acoustic/skull base/other CNS tumours Centralised multidisciplinary decisions (\pm treatment in hubs)		
Sarcomas	Symptoms Control Tissue Diagnosis Cyto Reduction	Maximal resection depending on site of tumour etc.
Overlap with Sarcoma MDT		

3.2 Oncological Treatment of Brain and CNS Cancer

Introduction

- This guidance has been written to provide guidance on the treatment of brain and CNS cancer in the East Midlands Cancer Network (EMCN)
- See network chemotherapy prescribing proformas for details of chemotherapy/anti-cancer regimens.
- All patients will be considered for entry into a clinical trial where appropriate
- All patients should be discussed within a multidisciplinary team meeting (MDM) before commencing initial treatment.
- All chemotherapy regimens listed within this document are delivered at:
 - Nottingham University Hospitals NHS Trust
 - City Hospital Campus
 - United Lincolnshire Hospitals NHS Trust
 - Lincoln County Hospital
 - United Hospitals of Leicester NHS Trust
 - Leicester Royal Infirmary
 - Northampton General Hospital
 - Royal Derby Hospitals NHS Trust
 - Royal Derby Hospital
 - Queens Hospital, Burton

Patients are referred from the neuro-sciences MDM. Typically they will have had a biopsy or debulking surgery. Subsequent treatment intent will depend on performance status, but early input of palliative care services is recommended in all cases.

Radiotherapy is the primary non-surgical modality of treatment. However, the addition of chemotherapy has been shown to improve outcome in selected patients with GBM.

High Grade Glioma

Glioblastoma multiforme (GBM) – Grade 4

- Following surgical debulking or biopsy patients of PS 0-1 up to the age of 70 can be considered for chemoradiotherapy using the Stupp regimen.
- Patients >70 with PS 0 will be considered on an individual basis given the increase in toxicity with this regimen.
- Patients up to the age of 70 with PS >1 will be considered for radiotherapy alone.
- Patients >70 with PS 1-2 will be considered for radiotherapy alone.
- Patients with PS 3-4 will be considered for active best supportive and palliative care.

All disease progression patients will be considered for further active treatment, usually chemotherapy but sometimes surgery has a role to play and patients will be reviewed by neuro-sciences MDM.

Chemotherapy

Stupp regimen (Chemoradiation followed by adjuvant treatment)

This regimen involves radical radiotherapy with concurrent chemotherapy with temozolomide (daily 75mg/m²) followed by 6 cycles of adjuvant temozolomide (usually at 200mg/m²/day days 1.5).

N.B. If a patient's full blood count is satisfactory at the end of treatment (Neuts ≥ 1.5 and PLT ≥ 75) and on day 28 post chemoradiation, start adjuvant temozolomide at 150mg/m² Cycle # 1. Four weeks later If FBC is within normal range then proceed to Cycle # 2 of 200mg/m². If FBC below normal limits continue with 150mg/m².

N.B. Temozolomide causes lymphopenia and hence patients should be given prophylaxis against PCP during the concurrent phase (e.g. with co-trimoxazole).

Palliative treatment

If patients have progressed during primary treatment further active treatment has a very low chance of benefit which must be discussed with the patient.

At disease progression following completion of initial active treatment, patients of good PS will be considered for further active treatment, usually chemotherapy but sometimes surgery has a role to play and patients will be reviewed by the neurosciences MDM.

Palliative chemotherapy will usually be with PCV but patients may be considered for any ongoing studies.

Gliadel® Implant in GBM

The Brain NOG do not support the use of concurrent chemoradiation for patients with GBM who have Gliadel® implants inserted into the tumour resection cavity as there is currently no data to support this. These patients will be considered for radiotherapy alone.

Glioma - excluding GBM - Grade 3

Radiotherapy is usually the first non-surgical treatment outside of clinical trials.

Young patients with large volume disease may be considered for primary chemotherapy outside of trials with the aim of delaying late radiotherapy toxicity.

At progression patients will be reviewed in the MDM to consider whether further surgical debulking is possible and then palliative chemotherapy options below.

Palliative treatment

Patients must be PS 0-2 to be considered suitable for palliative chemotherapy. Palliative care input should be reviewed on a regular basis.

1st line chemotherapy

- PCV – 6 weekly – up to 6 cycles

2nd line chemotherapy

- Temozolomide 150mg/m² – 5 days q28d cycle (up to 6 months)

3rd line chemotherapy

- Carboplatin single agent for patients performance status 0-2 who have had a previous good response to chemotherapy.

1.1 Low Grade Glioma – Grade 2

Radiotherapy if:-

- Tumour enlarging
- Symptoms
- Gemistocytic or pathology suggesting incipient transformation

Meningioma

Surgery is the primary treatment modality for meningioma. Elderly patients considered unfit for surgery are very unlikely to be suitable for radiotherapy as hypofractionated courses are not of benefit in meningioma.

Radiotherapy

External Beam

- Radiotherapy can be considered for patients with:-
 - Recurrent grade 1 following debulking surgery
 - Inoperable grade 1 or incompletely excised Grade I
 - Atypical meningioma (grade 2)
 - Malignant meningioma (grade 3)

Stereotactic

Patients are referred for stereotactic radiosurgery or stereotactic radiotherapy if lesions in eloquent areas – **following discussion at the MDT**

Systemic therapy

Chemotherapy and endocrine therapies have a small role to play but may be considered in individual cases. The use of endocrine therapy will be guided by progesterone receptor (PR) status.

Pituitary

Patients will be referred to the dedicated pituitary/craniopharyngioma MDT:-

Dr Peter Mansell
Contact details for referral:-
Diabetic Department
Floor C, South Block
Queens Medical Centre

Telephone Number:- 0115 9249924 Ext 63216

This MDT is held on a Wednesday – every four weeks.

Post primary treatment

Radiotherapy for:-

- Recurrence post resection
- Bulky residuum
- Persistent endocrine dysfunction

Craniopharyngioma

Post Primary Treatment

Radiotherapy for:-

- Postoperative residuum
- Recurrence

Primary brain lymphoma

At present all patients in EMCN with an initial diagnosis of CNS lymphoma is seen by Dr Eric Bessell in Nottingham.

Dr C Fox, Consultant Haematologist, based at Nottingham City Hospital administers chemotherapy to this group of patients and Dr K Foweraker, Consultant Clinical Oncologist, will be administering radiotherapy.

The East Midlands Cancer Network Chemotherapy Guidelines are on the website and can be found at:-

<http://www.eastmidlandscancernetwork.nhs.uk/HealthProfessionals-Chemotherapy-Oncology-BrainCentralNervousSystemTumours.aspx>

3.3 Palliative Care

Despite recent advances in diagnosis and treatment, primary brain tumours remain incurable for the majority of patients. These patients have significant symptoms and concerns, posing considerable burdens on relatives, carers and health professionals. Palliative care is co-ordinated medical, nursing and allied services for people with life-limiting disease, delivered where possible in the environment of the person's choice and which provides physical, psychological, emotional and spiritual support for patients and for patients' families and friends. The provision of hospice and palliative care services includes grief and bereavement support for the family and other carers during the life of the patient and continuing after death. A palliative approach involving attention to symptom control and the psychological, social and spiritual wellbeing of the patient and their family is relevant at all stages of the disease and especially in the terminal phase. Although focussing on quality of life, palliative care is also concerned with the quality of dying.

Palliative care utilises advance planning rather than crises interventions. It offers a multidisciplinary model of care that is focused on the whole person within their social and emotional context, rather than just the disease.

Standards for the provision of quality palliative care:-

- Care, decision-making and care planning are based on a respect for the uniqueness of the patient, their carer and family.
- The holistic needs of the patient, their carers and families are acknowledged in the assessment and care planning processes and strategies are developed to address their needs.
- Ongoing and comprehensive assessment and care planning are undertaken to meet the needs of the patient, their carers and family.
- Care is co-ordinated
- The patient, their carers and family have access to bereavement care, information and support services.
- Community capacity to respond to the needs of people who have a life-limiting illness is built through effective collaboration and partnerships.
- Access to palliative care is available for all people based on clinical need and is independent of diagnosis, age, cultural background or geography

3.4 Rehabilitation

Patients whose medical condition is stable should be referred to a rehabilitation service if they have ongoing problems affecting everyday life. Rehabilitation may include any of the following or a combination of:-

- Physiotherapy – focussing on a patient's movement, strength, coordination, balance and ability to walk.
- Occupational therapy – focussing on everyday tasks with a view to the patient becoming as independent as possible
- Social Workers – to improve the patients social situation and arrange access to services
- Speech and Language therapy – swallowing, communication etc.
- Clinical Psychologists

The EMCN Neuro-oncology Group adopt the principles of the National Rehabilitation Care Pathway for Brain and CNS Cancer:-

http://ncat.nhs.uk/sites/default/files/NCAT_Rehab_BrainCNS.pdf

Teenage and Young Adult Pathways

These pathways were discussed and adopted at the NDSG meeting held on 16th November 2012:-

11-1C-116k

The TYACN Pathway for Initial Management

The NDSG should agree, with the chair of the relevant TYACNCG, the TYACN patient pathway for initial management, including any features specific to the NDSG's cancer site and their host adult cancer network and incorporating their relevant MDT contact numbers.

The NDSG should distribute the pathway to the lead clinicians of the MDTs of their cancer site in their host cancer network.

11-1C-117k

The TYA Pathway for Follow Up on Completion of First Line Treatment

The NDSG should agree, with the chair of the relevant TYACNCG the TYACN patient pathway for follow up on completion of first line treatment including any features specific to the NDSG's cancer site and their host adult cancer network and incorporating their relevant MDT contact numbers.

4.0 The Follow Up Pathway

(Demonstrating Compliance with Measure 11-1C-108k)

Patient pathway attached as **Appendix 1**.

The follow up required varies between tumour types and will involve a combined approach to symptom management and disease surveillance.

Imaging is an integral part of follow up for patients with brain tumours and, ideally, it should be reserved for patients in whom the result of the scan is going to alter management. The frequency of scans is determined by the MDT.

Members of the neuroscience MDT held at Queens Medical Centre are responsible for deciding on the most appropriate surgical aspects for the management plan and adjuvant therapy for each individual patient based on neuropathological diagnosis. All other care including:-

- Chemotherapy
- Radiotherapy
- Co-ordination of supportive care

Follow up should be the responsibility of the cancer network MDT. Locally agreed guidelines for follow up are agreed locally.

The optimal frequency of follow up visits is determined by the patient's clinical condition. However, a routine follow up schedule of one to three monthly check-ups for patients with high grade disease and three to six monthly visits for patients with low grade disease is appropriate. The exact schedule will vary according to the patients condition.

Key points:-

- The aim of follow up for patients is to evaluate tumour control, monitor and manage symptoms from tumour and treatment and provide psychological support
- The optimal frequency of follow up visits is unknown and should be determined by the patient's clinical condition
- Follow up should be undertaken in a setting where the patient has access to members of the MDT
- The patient's GP is involved in caring for a patient with a brain tumour
- Co-ordinated care is the standard approach for caring for patients with brain tumours due to the complex needs involving several different specialists
- The patient should know which team member to contact at any time between visits.

Imaging follow up is included in the Imaging Guidelines (page 12).

5. Treatment of Brain Metastases

The spread of a primary cancer to the brain (cerebral metastases) is not uncommon. Although the incidence of the disease is not known, it has been estimated to occur in around 20 to 40% of all primary cancer cases. If a patient develops cerebral metastatic disease it significantly worsens their overall survival prognosis.

The Neurosciences MDT should review findings from neurosurgical biopsy and histopathological assessment. The results should be compared with clinical disease features and results from CT or MRI.

The responsible clinical team, usually the neurosurgical team, should provide the diagnosis in a face-to-face meeting with the patient and carers. The key worker is present at this meeting

Surgical Resection of Brain Metastases

Surgical Resection should be considered with or without whole brain radiotherapy (WBRT) for:-

- Isolated single metastasis where the risk of clinically unacceptable complications is low
- 1-2 metastases, in good performance patients with limited or no systemic disease
 - A meta-analysis has not demonstrated a significant difference in terms of survival between WBRT and surgical resection with WBRT
 - Consider tumour debulking, especially if it does not involve language areas of the brain
 - Consider complete tumour resection with wide margins if:-
 - Good performance status
 - Does not involve speech or language areas of the brain
 - Primary disease is under control

Radiotherapy for Brain Metastases

Radiotherapy should be considered:-

- WBRT as an alternative to surgical resection if surgery is not feasible

- Post operative radiotherapy – may prevent intracranial relapse
- Additional stereotactic radiosurgery (SRS) boost to the tumour site
- Stereotactic radiosurgery as an alternative to WBRT where there is a limited number of lesions of small size (less than 3 cm) and where histopathology is known
- A meta-analysis has not demonstrated a significant difference in terms of survival between WBRT alone and surgical resection with WBRT

This is the policy for East Midlands Commissioners for cerebral metastatic disease. This policy's structure is as follows:

- disease definition,
- local epidemiology,
- main treatment options,
- adverse effects and safety considerations [of treatment options]
- national policy context
- a review of the evidence of clinical effectiveness and statistical significance,
- existing treatment costs,
- cost effectiveness

This policy concludes with an East Midlands strategic commissioning statement on the identified treatment options for patients with cerebral metastases.

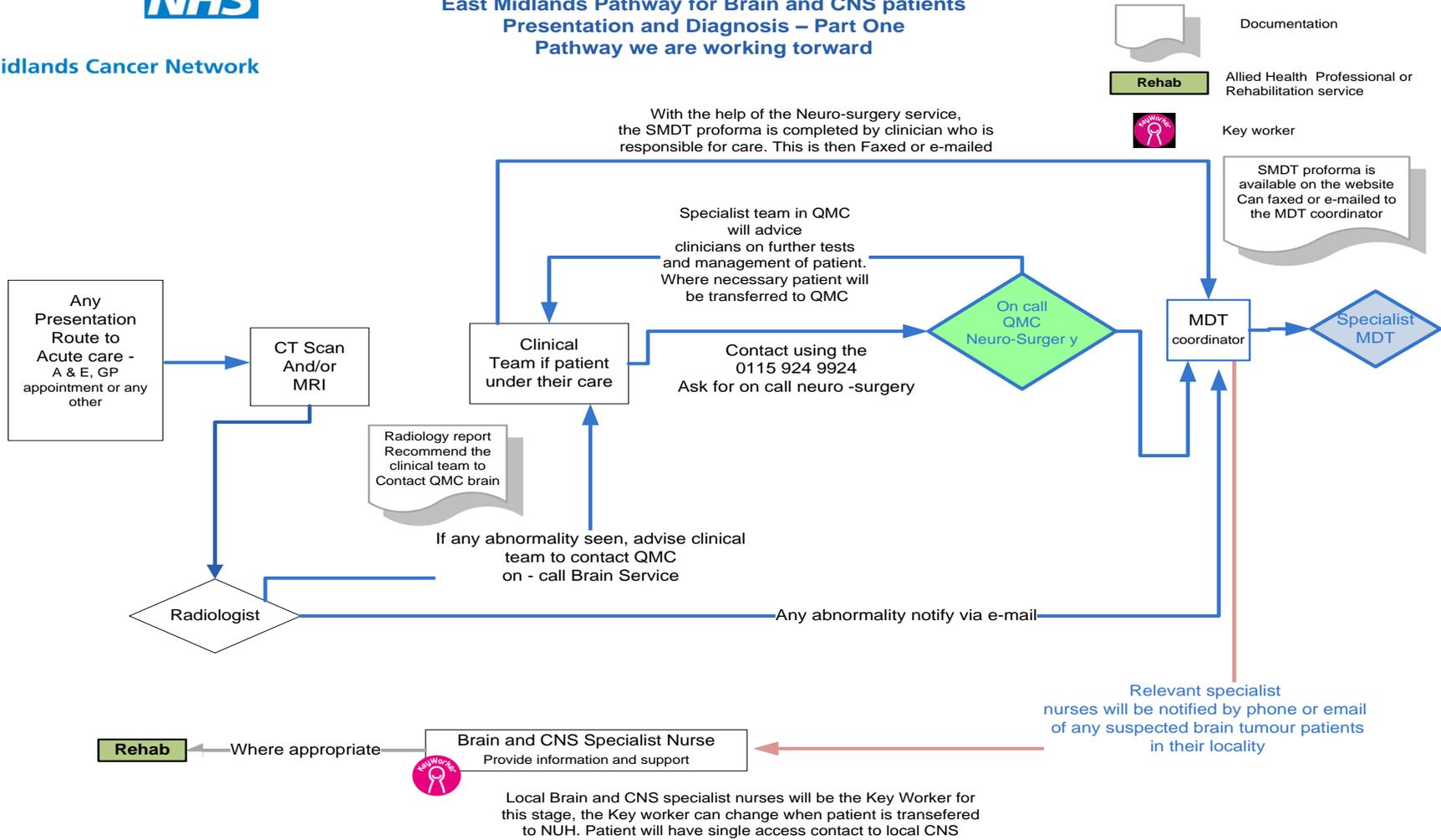
The **Treatment of Cerebral Metastases** agreed by the East Midlands Specialised Commissioning Group and the East Midlands Neuro-oncology Disease Site Group is shown in **Appendix 3**.

APPENDIX 1 – Patient Pathways



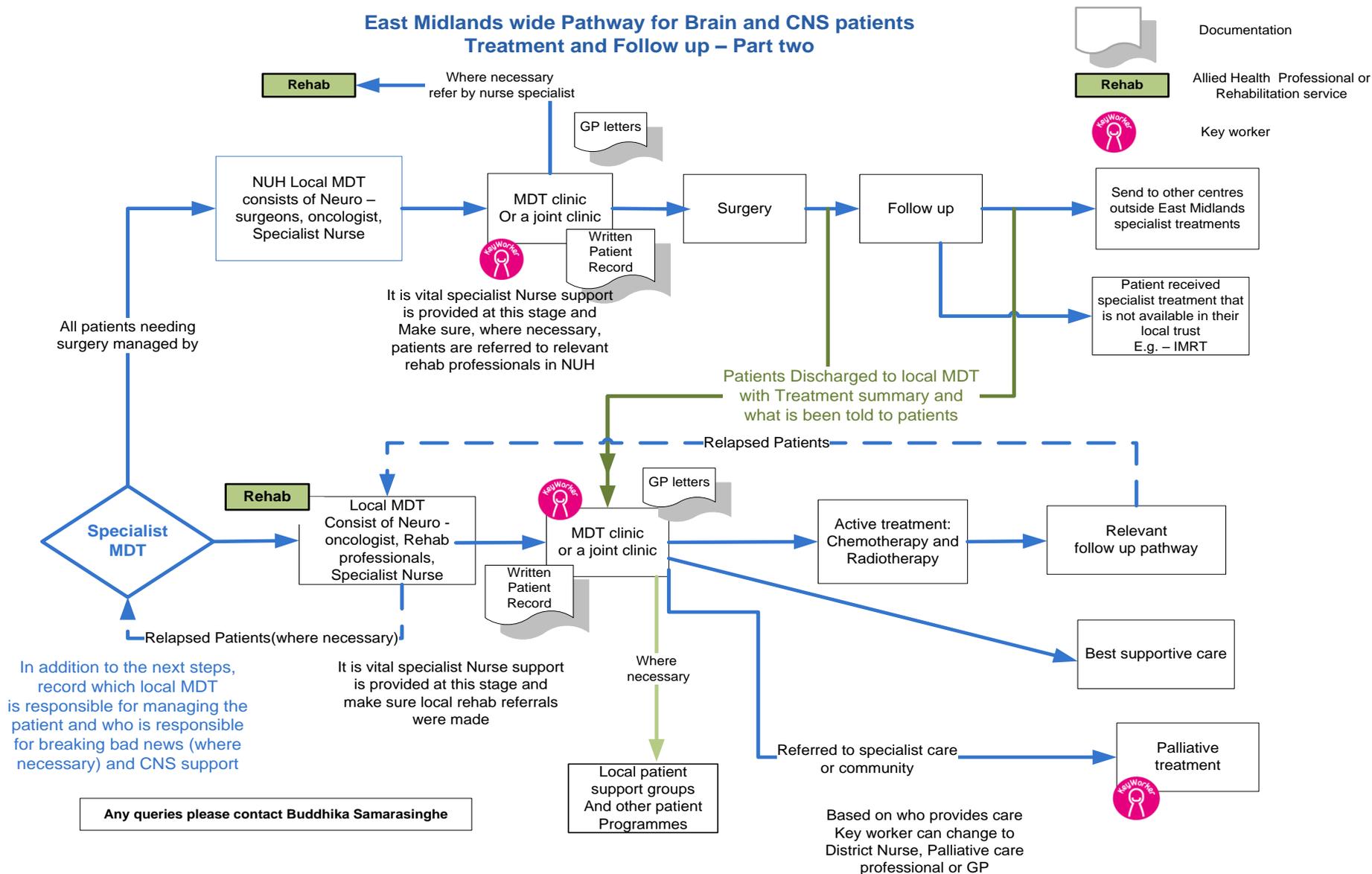
East Midlands Cancer Network

East Midlands Pathway for Brain and CNS patients Presentation and Diagnosis – Part One Pathway we are working toward



Any queries please contact **Buddhika Samarasinghe**

East Midlands wide Pathway for Brain and CNS patients Treatment and Follow up – Part two



APPENDIX 2

WHO Grading of Primary Brain Tumours

	I	II	III	IV
Astrocytic tumours				
Subependymal giant cell astrocytoma	•			
Pilocytic astrocytoma	•			
Pilomyxoid astrocytoma		•		
Diffuse astrocytoma		•		
Pleomorphic xanthoastrocytoma		•		
Anaplastic astrocytoma			•	
Glioblastoma				•
Giant cell glioblastoma				•
Gliosarcoma				•
Oligodendroglioma				
Oligodendroglioma		•		
Anaplastic oligodendroglioma			•	
Oligoastrocytic tumours				
Oligoastrocytoma		•		
Anaplastic oligoastrocytoma			•	
Ependymal tumours				
Subependymoma	•			
Myxopapillary ependymoma	•			
Ependymoma		•		
Anaplastic ependymoma			•	
Choroid plexus tumours				
Choroid plexus papilloma	•			
Atypical choroid plexus papilloma		•		
Choroid plexus carcinoma			•	
Other neuroepithelial tumours				
Angiocentric glioma	•			
Choroid glioma of the third ventricle		•		
Neuronal and mixed neuronal-glial tumours				
Gangliocytoma	•			
Ganglioglioma	•			
Anaplastic ganglioglioma			•	
Desmoplastic infantile astrocytoma and ganglioglioma	•			
Dysembryoplastic neuroepithelial tumour	•			

	I	II	III	IV
Central neurocytoma		•		
Extraventricular neurocytoma		•		
Cerebellar liponeurocytoma		•		
Paraganglioma of the spinal cord	•			
Papillary glioneuronal tumour	•			
Rosette-forming glioneuronal tumour of the fourth ventricle	•			
Pineal tumours				
Pineocytoma	•			
Pineal parenchymal tumour of intermediate differentiation		•	•	
Pineoblastoma				•
Papillary tumour of the pineal region		•	•	
Embryonal tumours				
Medulloblastoma				•
CNS primitive neuroectodermal tumour (PNET)				•
Atypical teratoid/rhabdoid tumour				•
Tumours of the cranial and paraspinal nerves				
Schwannoma	•			
Neurofibroma	•			
Perineurioma	•	•	•	
Malignant peripheral nerve sheath tumour (MPNST)		•	•	•
Meningeal tumours				
Meningioma	•			
Atypical meningioma		•		
Anaplastic/malignant meningioma			•	
Haemangiopericytoma		•		
Anaplastic haemangiopericytoma			•	
Haemangioblastoma	•			
Tumours of the sellar region				
Craniopharyngioma	•			
Granular cell tumour of the neurohypophysis	•			
Pituicytoma	•			
Spindle cell oncocytoma of the adenohypophysis	•			

APPENDIX 3 Cerebral Metastases Policy

The policy is accessible from the website of the East Midlands Specialised Commissioning Group;

[http://www.emscg.nhs.uk/ PoliciesandPublications](http://www.emscg.nhs.uk/PoliciesandPublications)